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INFECTIOUS HEPATITIS IN MASSACHUSETTS

With a Review of Present Knowledge of the Disease

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THE recent literature describing the experience of the armed forces with infectious hepatitis is voluminous, but reports on the disease in the civilian population have been few. This article summarizes our present knowledge of the disease and indicates how nearly our observations coincide with or differ from those of others. The clinical material used as the basis of this paper has been collected by means of visits to Massachusetts communities from which the disease has been informally reported to the Department of Public Health. Approximately 175 cases of infectious hepatitis were uncovered in Massachusetts in these investigations, but only 151 case histories are used in this report, since in the remaining cases 24 insufficient data were available to make their analysis reliable.

A short explanation of nomenclature in this disease will be useful. "Epidemic catarrhal jaundice" and "nonspirochetal infectious jaundice" are the terms that have been used in the past to designate it. "Infectious hepatic jaundice"[1] appeared as a title in 1937, when it was realized that the infection is localized in the liver rather than in the duodenum and larger bile ducts. At present the term "infectious hepatitis" — or with English authors "infective hepatitis" — is used to designate sporadic cases and "infectious epidemic hepatitis" for groups of cases during outbreaks. An occasional writer refers to infectious hepatitis as "hepatocellular catarrhal icterus"[2, 3] a term of doubtful value.

The limits of this discussion make it impossible to do more than mention the vast store of accumulating facts concerning artificially acquired hepatitis, which is in many ways identical with naturally acquired infectious hepatitis. Oliphant[4] has shown that the causative organism of infectious hepatitis is present in an infective state in the blood of patients with this disease.

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The term "homologous serum jaundice" is used to refer to hepatitis artificially acquired from any cause. The clinical picture produced by this condition is similar to that observed in infectious epidemic hepatitis.[5–8] The incubation period is different in the two diseases.[9–11] An attack of homologous serum jaundice does not protect against infectious epidemic hepatitis.[9, 12] It may be that there are separate etiologic agents for the two diseases.

At the present time, artificially acquired hepatitis appearing from a variety of sources is classified as homologous serum jaundice. Reports show that this disease has occurred after the use of certain lots of yellow-fever vaccine,[5, 13–17] measles antiserum[18, 19] and mumps convalescent serum.[20, 21] Hepatitis after transfusion [7, 14, 19, 22] is now a well recognized occurrence. Contamination of syringes by infected serum has been reported both from a diabetic clinic[23] and following the administration of antisyphilitic arsphenamine.[24–26]

HISTORY

The available medical literature contains many statements concerning jaundice of a contagious variety. Hippocrates knew and wrote of such a disease.[27] Letters between Pope Zacharias and St. Boniface in the eighth century A.D.[28] describe epidemics of jaundice. The American Civil War produced many cases of a disabling, highly contagious jaundice.[29] Pomeroy[30] in 1898 in Michigan and Leslie[31] in 1909 in Maine described outbreaks much like the one to be discussed herein. Cockayne[27] in 1912 in England wrote an impressive and complete report of the information and literature then available. His article contains speculation that is now known to be based on facts.

Much was written after the British had had experience with huge numbers of men sick with jaundice at Gallipoli and the Dardanelles in 1915-1916.[32–36] From these reports it is apparent that

Weil's disease was not yet understood. Willcox[36] in 1919 made a clear classification and separated epidemic catarrhal jaundice from other forms of contagious and noncontagious jaundice.[37–47] American observers showed an interest in outbreaks of jaundice, especially Williams,[48] Wadsworth[44] and Symmers[40] in New York State; Hiscock and Rogers[49] in Connecticut described its occurrence among college students in 1922. Blumer[50] presented an extensive study of what he called infectious jaundice in the United States in 1923. In that same year, Jones and Minot[51] published a careful clinical estimate of the disease, pleading for more attention to its extent and potential dangers. The English literature of the 1930's[52–59] contains scattered reports of outbreaks, as does the literature of other countries,[60–70] with a few American records.[71, 72]

One cannot be certain that all these outbreaks belonged in a single group, since the etiologic agent had not been discovered, but there does appear to be a basic pattern in the histories of such episodes. Since the outbreak of hostilities in the Mediterranean theater, the German,[73–75] Italian,[76] French,[77] British[78–80] and American armies,[81, 82] as well as refugees in Palestine,[83–85] have suffered serious morbidity from infectious hepatitis. The Navy has by no means escaped.[86–88]

Etiologic Agent

It is now held that infectious hepatitis is caused by a specific virus. This virus has not yet been grown in the laboratory. Swedish investigators[89] in 1938 believed that they had successfully infected swine with the causative agent of infectious hepatitis. This has not been confirmed. German authors[90, 91] claimed to have been able to make the organism grow in the chorioallantoic membrane of chicks. Other German workers[92] claimed that the organism could be passed to birds. This work is not convincing and has not been repeated. Cameron[93] and Van Rooyen and Gordon[94] tried without success to infect animals during their experience in the Middle East. Hoyle[95] in England tried every possible route in mice, guinea pigs and chick embryos but was equally unsuccessful. Paul and his group[12] have tried all the animals named, as well as monkeys, but have not been able to produce infectious hepatitis in any of them.

It has been possible to transmit infectious hepatitis to human volunteers. This has been done in England [10] and America.[12] It is now known that human volunteers can develop the disease following the parenteral injection of small amounts of infective serum,[4, 9] following ingestion of infective serum or feces[10] and following the spraying of infective feces into the nasopharyngeal passages.[12] Certain facts about the virus itself are also known. Havens[96] has shown it to be extremely resistant to heat and capable of passing through the finest filters. MacCallum and Bradley[10] have demonstrated that the organism remains actively infective after drying and after storage in the dried state up to fourteen months. Stokes et al.[97] have suggested that chlorination of water contaminated with the virus of infectious hepatitis attenuates but does not kill the organism. The virus may prove to be resistant to chemicals in the strengths in which they are ordinarily used for the purification of water.

Epidemiology

Age

Reports lead one to believe that infectious hepatitis, like other contagious diseases, may attack persons of any age.[46, 50, 55–57, 85, 98–100] The age distribution of the 151 cases collected in Massachusetts was as follows: under five years, 8.6 per cent; five to nine, 17.2 per cent; ten to fourteen, 17.9 per cent; fifteen to nineteen, 11.9 per cent; twenty to twenty-four, 6.7 per cent; twenty-five to twenty-nine, 9.3 per cent; thirty to thirty-four, 11.2 per cent; thirty-five to thirty-nine, 9.3 per cent; and over forty, 8.0 per cent. Persons between six and forty years of age are oftenest affected. The authors reporting on special age groups, such as college students[49, 101] and soldiers,[75, 80, 102–104] do not, of course, have a wide range, but health officers in England[55, 105] and physicians in rural communities in America[31, 50, 106] show a wider distribution of ages affected. Our observations in Massachusetts in 1945 suggest that different age groups are preponderantly affected in different communities within a single outbreak period. Community A in Massachusetts, for instance, showed a higher rate among young adults, although the population was not preponderantly of any particular age group, whereas Community C showed a far greater incidence among the children of early school age (six to ten years), in spite of the fact that adolescents and young adults were heavily exposed at school and in the home. Chance or the operation of unknown laws of susceptibility must account for this variation.

Sex

The disease affects both sexes practically equally. In our series, there were 71 males and 80 females.

Geographical Distribution

There is no question that infectious hepatitis has a world-wide distribution. For the reader's interest, references to a number of epidemics believed to belong under the heading of epidemic infectious hepatitis are cited.[27, 28, 32, 36, 37, 42, 43, 47, 60–63, 65–70, 76, 77, 107]

Incidence

According to the records, the incidence of infectious hepatitis has varied enormously. A workable concept is that this disease, like poliomyelitis, is always present in the form of sporadic cases. Epidemics take place from time to time and in various regions when natural conditions favor the growth of the virus and when artificial conditions of crowding

and poor conditions of all sorts exist. In 1898, Pomeroy[30] reported 676 cases among 30,000 persons in Michigan. Williams[48] reports 700 cases in the 1921 outbreak in New York State and considers this to be about 50 per cent of the known cases. Pickles[52] describes 250 cases in 5700 persons exposed. Rogers[101] states that the average number of cases at Yale University in a nonepidemic year is 22, and in an epidemic year he reports 63 cases within fifteen days.

Stowman[108] refers to infectious hepatitis as the "new disease" of World War II, without giving supportive evidence of its newness. The disease is reportable in the Scandinavian countries, Finland and Switzerland; these countries reported 65,000 cases in 1943. Army experience[80, 82, 109] is cited to give an idea of the extensiveness of the disease at present. The Navy[86–88] in the South Pacific reports infectious hepatitis, as have the German,[73, 75] Italian[76] and French[77] armies. Since the disease is reportable in only a few states in this country, we have no idea of its incidence. Blumer[110] writes that it is reportable in California and that 118 cases were reported in 1943 and 335 in 1944. Handy[106] encountered well over 100 cases in a small New Hampshire community of 2500 persons between October, 1944, and April, 1945. Between May and July, 1945, we encountered reports of 175 cases in Massachusetts.

Season

In this small series, patients had onsets in every month, the lowest number being 9 in August and December and the highest, 80 in April.[28, 30, 50, 55, 70, 75, 78, 85, 101–103, 111]

Immunity

Only speculation is possible concerning immunity following infectious hepatitis until a means is developed of determining whether a subject is having or has had the disease. The fact that the gamma globulin of blood pools apparently contains antibodies against infectious hepatitis[112] is suggestive of permanent immunity after an attack. Furthermore, the age group attacked — six to forty years — suggests that older persons have acquired immunity by a previous attack. A physician who has been in practice in the same community for over forty years recalls a series of cases that he attended thirty-one years ago that were identical in every way with those existing in 1945 in the same community. In only 1 case in our series was there a second attack. A woman teacher of forty-two years sick with the disease in 1945 gave a clear history of having had a similar clinical picture at sixteen years of age after exposure during an epidemic of so-called "yellow jaundice" in her schoolroom.

Period of Infectivity

Because of the epidemic possibilities of infectious hepatitis, it is important to know the period of infectivity. Bates[59] considered the period to be four weeks after the onset of jaundice, and Pickles[52] estimated it as eight days before and up to two weeks after onset. Pickles remarked that the period of infectivity must be short, because of his observation that new cases came at regular thirty-day intervals. It is now known from transmission experiments that blood serum and feces are infectious during the active stages of the disease.[43] More evidence on this point is accumulating.

Incubation Period

Transmission experiments prove that under controlled conditions the incubation period of infectious hepatitis is about thirty days.[10, 12] Reports of epidemics suggest that many factors determine the time between cases in uncontrolled environments. Cockayne[27] and Glover[55] put the period between cases as four days; Pickles[52] puts it at thirty-five days. Rogers[101] states that the period of incubation for his cases was three to nineteen days, with an average of seven. Cameron[93] estimates the time as one to six months.

In our observation in Massachusetts in 1945, the period between cases in a household varied so widely that there scarcely seemed to be a pattern. In one family, 3 children became ill within six days at two-day intervals; in another family there were eight days, fourteen days, twenty-two days and twenty-eight days between the 4 cases. In two families living in adjoining homes, there were 3 cases in one house and 2 in another, and between each case there was a two-month interval, except in the last case, in which there was a twenty-one-day interval after probable exposure. The shorter periods apparently represent infection from the same source with variation in dates of onset; the longer ones may represent incubation periods of secondary cases. Because the virus is hardy[96] and may survive in the environment as well as in the body of the patient or carrier, it is often difficult to trace the source of infection and thereby determine the day of exposure. It is our impression that many factors influence the rapidity with which the virus produces symptoms. Such factors are undoubtedly responsible for some of the variation in the length of the incubation period. Stokes's[97] work with chemical alteration of the virus leads one to speculate that the incubation period may be lengthened by unknown factors affecting the virulence of the causative organism.

Method of Transmission

The important question of the method of transmission has not yet been settled. Although it is difficult to trace cases to contact with other known cases, the fact that cases occur in groups points to person-to-person contact as a method of spread. In our own series, contact of patients with probably infected groups was recorded in 139 cases, leaving only 12 sporadic cases in which no such association

could be found. The kind of contact is shown in Table 1.

Blumer[50] made a similar classification.

From Table 2 it does not appear that a "clean" home is a guarantee that infectious hepatitis will not gain a foothold. It will be noted, however, that there is a preponderance of single cases in these homes. The same observation was made in regard to communities. Community A was suburban and prosperous, the homes were well kept, and the persons involved were for the most part conscious of sound health practice. Communities B and D were rural and less economically favored, the homes were less well cared for, and considerable ignorance and opposition to such public-health measures as milk pasteurization were encountered. Community C fell between, with a portion of both groups described. From Table 1 it appears that infectious hepatitis is independent of anything but the presence of the virus in the community, together with probable likely contact in the majority of cases, and individual susceptibility, since obviously not all those exposed in the six-to-forty-year group became ill.

Table 1. *Nature of Contact.*

Place	Family Contact	School Contact	Job Contact	Miscellaneous Group Contacts (party, meeting)
Community A	33	8	15	6
Community B	4	11	0	1
Community C	13	14	2	1
Community D	6	7	1	1
Totals	56	40	18	9

Table 2. *Number of Cases Occurring in "Dirty" and "Clean" Homes.*

No. of Cases in Household	No. of Households "dirty"	No. of Households "clean"
1	6	20
2	3	5
3	3	4
4	4	2
5	2	+0
6	1	+0
Totals	19	31

Some of the possible methods of transmission discussed in the literature should be noted.

Insects. Two observers[75, 104] thought that flies were important. Another writer[103] suggested bedbugs. The presence of infectious hepatitis at all seasons seems proof that except in rare instances of extremely bad sanitation insects are unimportant.

Fomites. There are no data that either prove or disprove the importance of contaminated articles. Since the virus is resistant to heat and chemicals,[96] infectious hepatitis may be transmitted by fomites. Suggestive circumstances are found in the fact that 2 of the patients with infectious hepatitis in our series were postmen who handled letters coming from a theater of war known to be heavily infected with the disease. We learned also of a woman with infectious hepatitis who in previous months had received daily letters from her son, who was sick in Italy with the disease.

Water. There are three reports dealing with water as the vehicle for the virus of infectious hepatitis. Fraser[54] in Canada believed that his epidemiologic observations, together with proved fecal contamination of the water supply, showed an epidemic of infectious hepatitis to have been water-borne. Hallgren[113, 114] in Sweden worked out a similar theory when an explosive outbreak appeared in an institution and a nearby village, both of which used water from the same contaminated reservoir. Neefe and Stokes[115] claim that an outbreak in a girls' camp was due to contamination of a well by the feces of a patient with infectious hepatitis introduced into the camp early in the season. They produced sickness simulating infectious hepatitis in one of a group of volunteers by feeding them water from the supposedly contaminated well in the camp.[116] Water seemed unimportant in our study, since there were multiple sources of drinking water, none of them convincingly contaminated. Cockayne[27] believed that water was ruled out by the evidence of infectious hepatitis in troops who were forbidden water and were given only tea to drink, yet among whom cases continued to appear.

Food. Rogers[49] and Blumer[50] thought that food might be the vehicle for the causative agent of infectious hepatitis. It appears certain that food-borne outbreaks have occurred in the past, because transmission experiments with volunteers have shown that the feces of active cases contain the virus of infectious hepatitis.[12]

Air. This has been the favorite explanation over the years.[27, 30, 55, 56, 59, 100, 116, 117] From early concepts of bad air and vapors to the concept of droplet infection through talking, coughing and sneezing, most observers urged this theory even before the presence of a specific virus was demonstrated. In our study, droplet infection has seemed an important method of transmission because of contact between cases without the sharing of food or water.

In summary, study of the literature and observation of 151 cases of infectious hepatitis in Massachusetts in 1944–1945 led us to conclude that the disease is probably transmitted in more than one way — by droplet infection, by contaminated food and perhaps by water.

The possibility that nonicteric patients are potential carriers is still unexplored. Until a definite way of making a diagnosis has been developed, the existence of such cases can only be a subject of speculation. Work with volunteers shows that there are undoubtedly nonicteric cases.[10, 12] These studies

further show that the excreta from such volunteer patients and from patients in the preicteric phase of infectious hepatitis will, if fed to susceptible persons, cause the disease, so that it seems more than likely that nonicteric cases exist, as observers have insisted. Their presence would help to explain the spread of the disease when it has not been possible to show contact. In view of their probable existence, it may not be necessary to postulate healthy carriers. Physicians whom we consulted commented on the unusual incidence of nonspecific vomiting and diarrhea in their experience during the past months, and one report[118] is suggestive. Housewives spontaneously reported the same occurrence in their homes and those of their neighbors coincident with infectious hepatitis. There may well be some relation that will become clear when the behavior of the virus of this disease is understood.

Pathology

Infectious hepatitis, or catarrhal jaundice as the disease was named until recently in this country, has been held to be an inflammatory process causing edema in the large bile ducts and the duodenum, thus accounting for jaundice and other evidence of obstruction to the normal excretion of bile pigment.[119] Cockayne[27] in 1912 pointed accurately to the relation between the disease and acute yellow atrophy. He suggested that a weakened liver made it simpler for the virus to attack that organ. In the years following this, the concept of catarrhal inflammation held sway. Throughout, some observers held the liver to be the site of disease. Jones and Minot[120] in 1923 brought out clinical evidence that pointed to the liver as the site of infection. Blumer,[50] also in 1923, reported a pathologist's finding in Buffalo, New York, to the effect that in 1921 there was more acute yellow atrophy than he had ever seen in one year. There was simultaneously a widespread outbreak of epidemic jaundice, as it was called. Experimental work by Himsworth and Glynn[121] is relevant to the present concept of the pathologic physiology of infectious hepatitis.

Knowledge of the pathologic process has recently become more certain.[122–124] The needle biopsy[125, 126] has been introduced and in time, according to reports, will prove a reasonable diagnostic procedure for widespread use. Dible[127] has reported, after considerable experience, that most cases are pathologically benign and that following recovery no changes in the liver cells are visible. A small group of his patients showed mild but definite residual zonal fibrosis. Another small group showed classic cirrhosis as an end result. The fatal cases show acute and subacute hepatic necrosis of all grades of severity. The present view is that the virus causes damage in the hepatic cells themselves and that the clinical picture of obstruction depends on the inability of the cells to handle the bile pigment.

Lucké[122] has presented in detail the autopsy findings in 125 fatal cases of probable infectious hepatitis. These cases occurred among men in the armed forces. The livers in all cases showed parenchymal cell damage of all degrees, ending in acute yellow atrophy. In 75 per cent of the cases the spleen showed hyperplastic changes. Some of the kidneys showed cholemic nephrosis. In a moderate number of cases, there was edema of the brain and a meningoencephalitis. Lucké mentions phlegmon of the intestinal tract. Lesions in the gastric mucosa of patients moderately ill with infectious hepatitis have been seen with the gastroscope.[128] Lucké's presentation suggests that infectious hepatitis may cause widespread damage in the body.

Clinical Characteristics

This report on infectious hepatitis is based on histories obtained from hospitals and physicians, supplemented by talks with the patients themselves. Of the 151 patients, 22 were cared for in the hospital and 129 in their homes. These cases have been classified as 117 undeniable cases of infectious hepatitis and 34 likely cases. The former patients presented a history of contact, a convincing clinical picture and jaundice, whereas the latter gave a history of contact and a medical history characteristic of infectious hepatitis but no visible jaundice. All these patients came from communities in which the disease existed in sufficient numbers to give acceptable epidemiologic ground for considering the presence of infectious hepatitis to be epidemic in character.

Character of Onset

The onsets presented varying pictures in length and character. There were 31 cases of grippelike onset and 52 cases of abrupt or gradual onset, presenting chiefly gastrointestinal symptoms. Seventeen patients complained bitterly of abdominal pain at the onset; 5 of these localized their pains specifically in the right lower quadrant of the abdomen, and in 3 of these cases appendectomy was performed; 10 patients complained of severe headache, and 7 of some backache at the onset. Twenty-two mothers spoke of apathy, listlessness and drowsiness on the part of their children at this stage. A striking feature was that the onsets varied from community to community, suggesting that the strain of the virus may vary from one location to another. In Community A, the onsets were largely gastrointestinal in character; in Community B and Community D, grippelike onsets with inflamed throats led physicians to think of disease of the respiratory tract. In Community C, we encountered histories of headache, sleepiness and apathy as characteristic of the onset. A diagnosis of poliomyelitis, a not unknown occurrence,[129, 130] was considered in 1 case.

The length of onset varied from a few days in 46 cases to two weeks in 16 cases and four weeks and

over in 4 cases. Handy[106] had a similar experience in 1945 in New Hampshire. He reported caring for patients who felt ill and had vague gastrointestinal complaints for two months, suggesting the possibility of peptic ulcer. We have collected similar histories. Eventually such patients developed the usual picture of infectious hepatitis. These observations go far toward explaining the reports of widely varying incubation periods. With long, vague onset periods, depending to a degree on the subjective reaction of the patient, and with many patients ill with infectious hepatitis who never seek medical advice, the incubation period and period of onset cannot be definitely described during an outbreak in general medical practice.

Precipitating Factors

Factors apparently operating to precipitate infectious hepatitis were striking. These may account for the apparent susceptibility of one or two persons exposed to the same degree as the other members within a family or the other pupils in a schoolroom. There are reports of dysentery,[33, 36, 111, 131–133] paratyphoid fever,[32] chilling,[31, 35, 102] respiratory infection[27, 48, 55, 59, 101] and alcoholic excesses[35, 80] as antecedent and important factors in outbreaks of infectious hepatitis in institutions and troops.

There were 44 cases of precipitating factors in this series. These included 10 cases of previous recent bacterial infection, 8 of a moderately large intake of alcohol, 15 of fatigue attendant on war work, 4 of pregnancy, 5 of recent moderate or large doses of sulfadiazine and 2 of striking dietary deficiency in children. It is relevant that in a family of several children the child who acquired infectious hepatitis was the one who had had chronic middle-ear disease or was recovering from one of the exanthemas. Another interesting observation was that in three homes in which only the father was sick he had been on night duty as well as daytime duty.

Character and Duration of Jaundice

The usual first sign of approaching jaundice is the appearance of bile in the urine. Thirty patients reported this symptom. The next step in most cases is a noticeable yellow tint in the scleras. The process may cease at this point, especially in children. We observed four families in which a parent had an easily recognized case of infectious hepatitis and a child, after a febrile onset, had only discoloration of the scleras for a few days. If the process is of sufficient severity, jaundice of the skin becomes evident and may last from two days to a matter of weeks, the average being two weeks. The duration of jaundice in this series is shown in Table 3. When the jaundice disappears, it goes in the inverse order, bile appearing in the urine transiently in the convalescent period. If the jaundice persists for over three weeks, some other diagnosis than infectious hepatitis must be considered. When other diagnoses are ruled out, it is reasonable to consider that irreversible changes in the liver may be taking place[120] and that in a few cases these will end in fatal acute yellow atrophy.

Allied Symptoms and Signs

For clarity, the allied symptoms and signs encountered in infectious hepatitis are listed in Table 4 in order of frequency of appearance. In general, the subjective complaints begin to disappear with the appearance of jaundice. This does not hold true in the severer cases. It should also be emphasized that many patients are encountered in an epidemic group who have virtually no symptoms except mild jaundice. We saw cases in family outbreaks so mild that no physician had been consulted.

Some of these symptoms and signs are interesting enough to deserve separate comment. Sore breasts and menstrual irregularities may be due to disturbances in steroid excretion by the liver as a result of hepatic-cell dysfunction.[134] Edema can probably always be demonstrated at some stage in a case of infectious hepatitis. Lucké's[122] report brought out the frequency of ascites and edema of the brain in fatal cases. Cockayne[27] in 1912 reported diuresis as defervescence of the disease begins. Williams[135] has commented on this in his observation on hospitalized cases of infectious hepatitis. In the 32 cases with involvement of the central nervous sys-

TABLE 3. *Duration of Jaundice.*

DURATION	NO. OF CASES
Less than 1 week	10
One week	32
Two weeks	29
Three weeks	16
Four weeks	5
More than 4 weeks	4

TABLE 4. *Symptoms and Signs Other Than Those Associated with Jaundice.*

SYMPTOM OR SIGN	NO. OF CASES
Anorexia	75
Vomiting	65
Fever	62
Nausea, without vomiting	51
Symptoms of central nervous system	32
Abdominal pain	25
Diarrhea	13
Headache	10
Backache	7
Pruritus	6
Sore breasts	3
Menstrual irregularities	3
Difficulty in reading	3
Cough	2
Urticaria	2
Ankle edema	2
"Rash"	1
Herpes labialis	1
Herpes zoster	1
Periorbital edema	1

tem, the symptoms include irritability, apathy, drowsiness, stiff neck, temporary delirium and depression. These, with the 10 cases of headache, constitute an appreciable group of the 151 cases of infectious hepatitis. The literature reveals that other observers[31, 129, 130] have encountered such symptoms. Lucké[122] suggests that the loss of detoxifying power of the liver may well account for these frequently encountered symptoms. The occurrence of a rash has been previously reported,[31, 80] as have cases of urticaria.[28, 136] No explanation has been offered. With the well known occurrence of herpes labialis and a concomitant infection, it is surprising that only 1 case was encountered. We know of no reason why pruritus was so infrequent.

Severity

We were struck, as others[28, 30, 70, 106, 136] have been, with the increase in severity of infectious hepatitis with age. This was not without exception, since 3 men kept at their jobs with no apparent immediate ill effect during ten days of jaundice, whereas 2 children were ill for five weeks and complained of vomiting and epigastric pain long after clinical jaundice had subsided.

Pregnant women were especially ill, as others[50, 70, 85, 137] have noted. When one bears in mind the relation between infectious hepatitis and acute yellow atrophy and considers the fetus as an extra load for the liver, this observation is understandable. In our series there were 4 pregnant women. Two were delivered four to six weeks before the expected date. One of these women had a violent onset of infectious hepatitis, which the attending physician properly considered a toxemia of pregnancy. The diagnosis of infectious hepatitis was established on clear epidemiologic grounds. One woman aborted in the tenth week of pregnancy. One woman in her third month did not abort but had a violent and prolonged attack of infectious hepatitis, which she acquired from her daughter.

Alcohol may play a part in increasing the severity of an attack of infectious hepatitis. Damodaran and Hartfall[80] thought that this might well be the case. Observations made of protein-starved livers of famine victims in India suggest that dietary deficiency may, if severe enough, predispose to a serious attack of infectious hepatitis.[121] Drugs and industrial poisons, known to be specific liver toxins, should prove important in altering the course of infectious hepatitis.

Nonicteric Cases

Liver-function tests on volunteers[12] given infectious material show that there are undoubtedly persons who demonstrate evidence of hepatic disease without developing clinically recognizable infectious hepatitis. We have included 34 such patients in this series. The onset of their disease may be identical with that of typical infectious hepatitis. Usually bile can be demonstrated in the urine, but this occurs at times in many infections. These patients may have symptoms of gastrointestinal distress, marked anorexia and weight loss, but they never develop visible jaundice.

Physical Signs

A characteristic physical sign besides jaundice is enlargement and tenderness of the liver edge.[28, 51, 70, 120, 138, 139] We encountered such a finding in 10 cases. The pulse is not characteristically slowed.[50] The spleen is enlarged in 5 to 40 per cent of cases.[59, 70, 83, 138] Lucké[122] noted enlargement of the spleen in 75 per cent of his fatal cases. Barker et al.[82] report lymph-node enlargement, a finding that we never encountered. If the disease progresses to definite jaundice in a given case, the stools become clay-colored, as in obstructive jaundice from any cause. Edema may be present.

Laboratory Findings

Physicians caring for cases in our study used the foam test to demonstrate biliuria early in the disease. Twenty-six positive reports of biliuria were noted by them. Barker et al.[82] have used the methylene-blue test. Albuminuria is occasionally found, perhaps simply as part of an acute febrile illness; it was encountered in 7 cases in this series. Lucké[122] reports renal changes in fatal cases that he considers due to a cholemic nephrosis. Another report[140] notes cases of nephrosis in an epidemic of infectious hepatitis.

Hospitalized cases that can be carefully followed show a rise in bile pigment in the blood as the disease progresses. The level of bilirubinemia is the best index of the severity of a given case of infectious hepatitis. Liver-function tests, used in a wide variety, show changes that vary considerably.[82, 138, 141–144] These tests are not definitely useful, since they do not parallel the clinical status of the patient. An increase in prothrombin time, especially with a poor response to vitamin K therapy, is indicative of a bad prognosis. In our series, no evidence of hemorrhagic tendency was noted. In reports of epidemics, hemorrhagic events have been noted in severe cases.[40, 70, 80, 82, 136] Lucké[122] reported that 109 of his 125 fatal cases showed some evidence of hemorrhage.

The white-cell count is of some value in diagnosis at the onset, when it may rise to 10,000 to 12,000. As the disease progresses, the count falls to a normal level of 8000 and occasionally to 4000. There is a relative lymphocytosis throughout the illness. Jones[51] has discussed this, and Barker, Capps and Allen[82] recently presented their findings, as have earlier observers.[35, 58] The sedimentation time is not helpful.[145, 146]

Differential Diagnosis

During the onset, a diagnosis is difficult, since a specific test is lacking. Acute disease of the upper

respiratory tract, grippe, influenza, an atypical pneumonia, enteric infection such as dysentery, acute appendicitis[28, 35, 59, 117] and infectious mononucleosis come to mind. In the presence of an epidemic series of cases of infectious hepatitis, however, the problem is relatively simple. The white-cell count during onset is helpful, especially in ruling out acute appendicitis. It is elevated to levels around 20,000 in Weil's disease, which usually presents a more serious clinical picture from the start, and the specific organism *Leptospira icterohaemorrhagiae* can be found in the blood.

Infectious mononucleosis may produce jaundice.[147] If done at the right time, heterophile agglutination with sheep's cells will decide this point. In the tropics, malaria and sandfly fever have to be differentiated.

Sequelae

The convalescent period varies with the severity of the given case, together with the age and temperament of the patient. In young adults, we obtained uniform histories of weakness, fatigability and loss of energy as characterizing convalescence. This period ranged from two weeks to four months, with the average about one month. This time of disability was a serious problem for the armed forces both in naturally acquired infectious hepatitis[82] and in hepatitis occurring after the giving of yellow-fever vaccine[8] and blood transfusion.[7]

Return of the appetite was often slow. In the absence of laboratory aid, this symptom is of distinct help in estimating the return of liver function to normal. Mothers remarked of their convalescent children — and 6 adult patients agreed — that when the appetite did return it was practically impossible to give the patient enough to eat.

Weight loss was a striking feature of infectious hepatitis, as others[82, 106] have noted. In the 47 cases in which a sufficiently reliable history was obtained, there was a weight loss of five to ten pounds in 20 cases, of ten to twenty pounds in 24 cases and of thirty pounds in 3 cases.

Relapses took place in 4 cases, with a return of jaundice in 2 of them and a prolonged period of biliuria in 2. Returning to work too soon was the explanation in all these cases. Barker, Capps and Allen[82] have done considerable work on this point. It is an important one for civilian physicians to consider, with diminished liver function in mind as a sequela. Altschule,[139] Kornberg[141] and Rennie[144] have done careful laboratory work with patients who have recovered from infectious hepatitis and in normal controls. Their results suggest that a certain number of patients emerge from an attack of infectious hepatitis with some inpairment of liver function. This work also suggests the significant fact that the impairment may not parallel the clinical course of the attack. Caravati[148] describes the so-called "post-hepatitis syndrome."

Prognosis

The mortality figures of different epidemics have been carefully reviewed by Lucké,[122] who gives the range as 0.24 to 0.44 per cent. Stowman,[108] in his recent report of present-day infectious hepatitis, reports the death rate as ranging from 0.1 to 1.0 per cent. In the present series there was 1 death. This occurred in one of a small series of cases in an institution after three days of clinical illness, during the last twenty-four hours of which the patient was in a coma. Autopsy showed complete hepatic necrosis. Cockayne[27] reported such cases.

Treatment

General Management

Dietary management has been the standard weapon in the care of infectious hepatitis. Dible et al.[127] report histologic evidence of damage and isolation of hepatic cells from their columns in the early phase of infectious hepatitis, following which the cells can be shown to be without glycogen. Jones[149] considers a high sugar intake extremely important as protection for the hepatic cells. Certainly in severe cases, nausea and vomiting are dramatically relieved by intravenous dextrose in concentrations of 5 to 25 per cent. Observations made in the present series show that a high intake of sugar by mouth was the most satisfactory measure subjectively, a daily intake of 300-400 gm. of carbohydrate being a reasonable goal. It is best given by mouth whenever possible.

Barker, Capps and Allen[82] think that a high protein intake is important and quote György's[150] work. British workers[151, 152] are not satisfied that high protein feeding alters the course of the disease. Handling of proteins is one of the liver's foremost and most complicated tasks, and it may be best not to give the liver large doses of protein to handle while it is disabled.

Barker, Capps and Allen remark that the matter of low fat intake is not yet settled. Experience shows that, except in the most benign cases of infectious hepatitis, the gastrointestinal tract cannot easily handle fat. Bile is being excreted with difficulty and in some cases not at all, so that fat digestion is impaired.

Vitamin K need only be added in the event of an attack of infectious hepatitis sufficiently severe to change the prothrombin level. In this series, the only evidence of unusual bleeding was a history of flooding during the menstrual flow, which was coincidental with the period of jaundice of 3 women having infectious hepatitis.

Jones[149] stresses the use of adequate doses of the vitamin B complex during the acute and early convalescent phases of infectious hepatitis, because the liver is temporarily unable to act in the synthesis of this vitamin. Barker, Capps and Allen,[82] on the basis of György's experimental work, believe that too much vitamin B may be harmful.

We should like to point out that the widespread use of sulfonamide compounds at the onset of all acute infections may be injudicious in the event that the case proves to be one of infectious hepatitis. The liver acts as a detoxifying agent in handling these drugs. If, as transmission experiments with volunteer subjects suggest, the liver function is impaired before the onset of clinical symptoms,[12] use of the sulfonamides is certainly contraindicated. Perhaps these drugs can act as a precipitating factor. To illustrate this point, reference may be made to a family in which 5 of the 12 children had infectious hepatitis. The mother called one physician for 3 of the sick children and another physician for the other 2. The former were treated with a mild cathartic, a high intake of sugar and bed rest, with prompt recovery. The latter, given large doses of a sulfonamide in the onset period, had to be hospitalized and had jaundice of longer duration than did any other patients of the same age group in this series. This observation is certainly suggestive that the sulfonamide drugs should not be administered in infectious hepatitis.

Morphine and the barbiturates should be used cautiously in severe infectious hepatitis, because of the presence of active liver disease. Calomel and violent purges are only mentioned to be dismissed, as belonging to the days when infectious hepatitis was thought to be an ascending cholangitis and duodenitis, with swelling around the ampulla of Vater.[119]

Prophylactic Treatment

A new chapter in the management of infectious hepatitis is opening with the use of gamma globulin, the antibody fraction of plasma employed in the attenuation of measles. It is of no proved value therapeutically.[153] Stokes and Neefe[154] believed that they had used it successfully in the summer of 1944 to halt the progress of an epidemic of infectious hepatitis in a girls' camp. Recent reports by Gellis et al.[112] suggest that gamma globulin confers passive immunity against infectious hepatitis for at least six to eight weeks. Prevention is desirable for pregnant women, as has been indicated. Modification will be sought as in measles because of evidence that one attack confers immunity, with few exceptions. We gave modifying doses — 0.25 cc. per pound of body weight — to the members of two families in Community A who were heavily exposed to infectious hepatitis by immediate family contact. Three of these subjects had episodes eight weeks later, suggesting that they were having modified infectious hepatitis. In one family in which 3 persons were given gamma globulin, a baby of nineteen months had a slight fever, was peevish, refused to eat and had light-colored stools for three days, whereas two other small children in the family, recently recovered from infectious hepatitis, — were not sick at the time.

Supplies of gamma globulin will become available to Massachusetts physicians if further study confirms its usefulness in prevention and modification. American plasma has been used in controlling epidemic infectious hepatitis in the Mediterranean theater.[112]

Summary

Infectious hepatitis occurs sporadically and in epidemic form over a wide geographical area. It seems certain that the disease is caused by a specific virus with an apparent affinity for the liver. The disease in most cases confers lifelong immunity.

The transmission of infectious hepatitis, on the basis of present knowledge, takes place by contact of a susceptible person either with a patient having the disease or with material contaminated by the causative virus. It seems certain that the virus can be carried in food. It may be carried in water.

The findings in 151 cases of infectious hepatitis in Massachusetts occurring during 1944–1945 are presented and discussed.

A plea is entered for the recognition and careful handling of infectious hepatitis. This disease clearly may cause irreversible liver changes. Our observations lead us to believe it is a serious disease in pregnant women.

Gamma globulin has no place in the treatment of the active phase of infectious hepatitis. It has been shown to be capable of producing passive immunity of six to eight weeks' duration and should be useful in the control of small outbreaks. Further study may prove that gamma globulin given during the incubation period can modify infectious hepatitis, in a manner similar to its action in measles.

An attempt has been made to include all references to epidemics of jaundice that, in the light of present knowledge, may be designated as infectious (epidemic) hepatitis. References to foreign articles, not read and not available, are included for their interest in showing the incidence and wide geographical distribution of this disease.

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MODERN GOVERNMENTAL MEDICAL PROBLEMS*

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MY brief remarks will be made from the viewpoint of one who has spent his life in the Army Medical Corps. This viewpoint, however narrow, has been broadened by the experience of two wars and the intimate association in them with mobilized civilian medicine and, between wars, a more limited association with my civilian colleagues. This country has just been through not only the biggest war in its history but also the biggest medical operation in the history of the world. I believe that everyone can profit by reviewing this experience. My comments will be limited to a review of a few crucial aspects of the Army's medical service. I shall touch on the medical problems confronting the Government as a whole and suggest one or two points of contact between the Government and civilian medical practice.

First, as to the Army, few realize that the total number of patients in all Army hospitals in 1938, both in the United States and overseas, totaled less than 10,000, which represented during this war the patient load at a single large Army medical center. With troops in the prewar period widely dispersed and with a total of only 10,000 patients, it was clearly impossible for the Army to develop a high degree of medical specialization. We did the best we could by evacuating patients who required specialized treatment to general hospitals. This made it possible for the Army to keep some personnel at a high pitch of skill by affording them the quantity and variety of clinical material that is essential for the practice of specialized medicine.

During the war approximately 15,000,000 patients were admitted to some twelve hundred Army hospitals. For two years, between 1943 and 1945, the number of patients in hospitals was never below 270,000, and there was a peak load in April, 1945, of 544,000. At the start of the war the Army Medical Corps was slightly in excess of 1000 doctors. This number was expanded until some 47,000 were on duty. Despite the availability of these doctors, we were severely pressed for specialists and in many crucial areas simply did not have enough to go around — this in spite of the most careful supervision to see that every doctor was placed where his ability could be utilized to the fullest. As an example of this supervisory endeavor, when the hospitals in this country were busiest, a careful study by Brigadier General Fred W. Rankin showed that every board member in the surgical specialties was actually practicing in his specialty or acting as a consultant in the Office of the Surgeon General or in one of the geographical-area service commands. This scarcity of trained specialists made it necessary to organize all the general hospitals in approximately twenty specialty centers, such as those devoted to neurosurgery, ophthalmologic surgery, amputations, thoracic surgery, psychiatry, plastic surgery and tropical medicine, and to concentrate our key personnel at them. Patients requiring specialized care went to these centers, where qualified staffs were available. The success of this intricate system depended on a highly efficient medical regulating mechanism for distributing patients speedily and correctly. As many as 57,000 patients returned from overseas within a single month. Each patient was sent to the general or convalescent hospital suitable for his treatment and nearest his home.

Despite this concentration of specialists and patients, the shortages in skilled personnel were sufficiently marked to force the Army to engage in an extensive training program. Outstanding in this respect was the training of neuropsychiatrists; the Army more than doubled the numbers from civilian life. Since tropical medicine was an esoteric field, the Army had to train almost 100 per cent of the doctors used in this division. Large numbers of younger men were given training courses in anesthesia and radiology, as well as in other branches of medicine.

In this system of specialized medicine the supervision of patients and the assignment of personnel were largely the responsibility of our consultants. These men were chosen carefully and given a great amount of authority. There were consultants not only in the office of the Surgeon General but on the staffs of each major force. I regret to say that almost without exception these men who served so well during the war have now returned to civilian life. We have all realized the large contribution that they made and the benefits that were derived from their work. The high achievements and the outstanding professional advancements made during the war were dependent to a marked degree on the development and operation of this consultant system. We realize that a small postwar Army cannot possibly justify the full-time assignment of a large number of key specialists. We have, therefore, taken steps to develop a consultant system that will utilize civilian experts on a part-time basis.

You may also be interested in our plans for professional training. After the last war, our numbers were too small to permit more than a few men to continue with their studies outside Army facilities. This time we are seeking to provide adequate numbers so that a considerable part of the Medical Corps can at all times be away at school or otherwise pursuing postgraduate training. In passing, it is

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of interest that the Surgeon General has recommended and the General Staff has approved financial incentives for men who have been passed by their specialty boards.

The Army's situation can be summarized in the following terms. We developed during the war a highly specialized type of medicine, which was the principal reason that we were able to furnish such excellent medical care to the sick and wounded. We are doing our utmost to perpetuate this system in peace.

Now a word concerning the medical service of the federal government as a whole. The various governmental agencies have been largely independent in thought and action, but there has always been some integration among the medical services of the Government. In prewar days the Army provided medical care for a considerable number of patients of the Veterans Administration and was also responsible for the medical care of members of the Civilian Conservation Corps.

During the war the medical services of the Army and the Navy went their own way, except in theaters of operations. There it was made evident that some integration of available means was definitely necessary. To a limited extent, Army and Navy hospitalization and evacuation operations were combined, with mutual satisfaction and effectiveness in parts of some theaters. At present, both the Army and the Navy are doing what they can to assist the Veterans Administration, which has an acute shortage of beds and personnel. For instance, the Army is holding all patients with tuberculosis who would ordinarily be discharged from the service to the Veterans Administration. We have made approximately 10,000 beds available in Army hospitals for the care of veterans.

I have studied the problem of the possibility or desirability of integrating, in whole or in part, the federal hospitals. Boston with its environs is typical of many large areas in this country. Here there are Army, Navy, Veterans Administration and Public Health Service hospitals — each operating independently. Here also there are state, county and city hospitals and large civilian teaching institutions. If we are to make the best use of our limited governmental resources, in fact of our limited national resources, it seems appropriate — at least to me — that the activities of these separate systems be somehow co-ordinated, correlated or integrated into governmental medical centers for the care of patients entitled by law to governmental medical aid. Perhaps we should establish specialty centers, transfer patients accordingly and assign our specialists not in terms of the service to which they belong but to the hospital designated for their specialty at the same time utilizing to the full the staffs and facilities of the civilian teaching institutions. This should result in better treatment of patients. A combination of these independent facilities with their physical means and their co-ordinated staffs would provide an educational nucleus for the successful training of interns, residents, nurses and technicians for governmental service and should add to the attractiveness of a governmental medical career. As an integral part of such a medical center, there would be a central diagnostic and treatment clinic through which all except emergency patients would funnel and where the all-important outpatient treatment could be concentrated.

A significant finding in this brief study is the marked discrepancy between the available and required numbers of specialized personnel. There is no prospect whatever, so far as I can see, for the four federal agencies, operating independently, to meet their full responsibilities for hospitalization through the employment of full-time staffs. If these responsibilities are to be met, — and I am sure that each of us believes that they must be met,— the old barriers between governmental and civilian medicine must be broken down. As you know, the medical director of the Veterans Administration is seeking the assistance of medical schools and of the civilian medical profession to the greatest possible degree. The Army is looking forward to seeking the assistance of civilian consultants on a part-time basis. In short, the period of complete isolation and self-sufficiency appears to be ending.

The Army, the federal government and in fact American medicine at large face a host of serious medical problems. A preliminary review of governmental medical requirements and means indicates that we shall be hard pressed, at best, if we are to advance as rapidly as we should. Surely there is no room for the inefficiencies of isolation. The successful solution of a problem involves not only good will but intensive study. The good will of all of us exists in the attempt to solve the problems confronting governmental medicine. I believe that intensive study is needed.

ACUTE POLIOMYELITIS IN PREGNANCY*

Its Occurrence according to the Month of Pregnancy and Sex of Fetus

W. Lloyd Aycock, M.D.†

BOSTON

A CLINICAL impression that poliomyelitis occurs with undue frequency during pregnancy and its possible importance in relation to susceptibility have been emphasized in previous papers.[1–4] There are many reports of cases in the literature that deal with various aspects of the disease in the pregnant mother, such as effects of the disease on the mother and the fetus or obstetric problems created by the occurrence of the disease. Few reports have dealt specifically with the question of frequency of the disease in pregnancy or its significance. Within the age groups concerned pregnancy is relatively frequent and poliomyelitis is infrequent. For this reason it is difficult to establish any association between the two conditions on the basis of frequency alone. Comparisons of the percentage of cases that occur in pregnant women with the estimated percentage of women of corresponding ages who are pregnant at any given time, as calculated from birth rates, have indicated an increased occurrence of the disease during pregnancy. In an outbreak in Detroit in 1939, in which the expected chance occurrence was 0.95, 4 cases were observed in pregnant women. Eleven of the paralyzed women were over the age of twenty, and in 3 of these cases (27 per cent) paralysis developed during pregnancy.[4] This is the first study in which a record concerning pregnancy was obtained in all cases of the disease. In data obtained through the co-operation of health departments of sixty-three cities or counties in fifteen states, including Massachusetts, and in the District of Columbia, with an expected occurrence of 58 cases in 1944, 73 cases were listed. In all but two of these areas the data available on pregnancy were known to be incomplete. For one of them, the District of Columbia, the number of expected cases in pregnancy based on birth rates for the registration area — probably too high a figure for Washington — was 1.8. Of the 18 cases in women of twenty to forty-five years of age, 4 (22 per cent) occurred during pregnancy. In Duluth, Minnesota, there were 8 cases in adult women and 1 of these patients was pregnant; the expectancy was 0.8 per cent. Fox and Sennett[5] report that of 6 women with poliomyelitis admitted to South View Hospital, Milwaukee, 4 were pregnant. These authors also review earlier reports such as that of Brahdy and Lenarsky, which showed that of 15 admitted women over the age of nineteen, 3 (20 per cent) were pregnant.

Waaler[6] has recently reported that of 23 women over eighteen years of age who had poliomyelitis in 1941, in an outbreak at Bergen, Norway, 7 (30 per cent) were pregnant, as compared with an estimated pregnancy rate for women in the same age group in the same locality of 6.4 per cent.

Through the co-operation of the Division of Communicable Diseases of the Massachusetts Department of Public Health, it has been ascertained that 10 of the 54 women between fifteen and forty-five years of age with poliomyelitis in 1945 were pregnant (Table 1). Actually, the question of pregnancy was verified in only 40 of these cases.

All these studies relating to the frequency of poliomyelitis concern numbers of cases too small to be convincing in themselves. In this respect the study of the question presents a problem similar to that in poliomyelitis following tonsillectomy. The relation of tonsillectomy to poliomyelitis became evident not on the basis of the actual frequency of its occurrence but from the localized occurrence of

Table 1. *Poliomyelitis during Pregnancy in Massachusetts (1945).*

Age	No. of Female Patients	Estimated Percentage Pregnant	No. of Expected Cases in Pregnancy	No. of Checked Cases	No. of Corrected Expected Cases in Pregnancy	No. of Observed Cases in Pregnancy
yr.		%				
15–19	14	3.55	0.497	6	0.213	0
20–24	16	10.58	1.693	16	1.693	3
25–29	8	8.56	0.685	6	0.514	3
30–34	12	6.46	0.775	9	0.581	3
35–39	2	4.18	0.084	2	0.084	1
40–44	2	1.66	0.033	1	0.017	0
Totals	54		3.767	40	3.102	10

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a particular type of the disease (bulbar poliomyelitis) at a specific interval following tonsillectomy.[7, 8] Similar evidence of localization is seen in data collected over a period of years from various sources on cases of poliomyelitis in pregnancy.

In my records there are 236 cases in which the month of pregnancy in which the disease occurred is known, and 9 cases in which it occurred from two to twenty-three days after delivery, which is within the range of the incubation period of the disease. There is no indication of a tendency of the disease to occur at any specific period of pregnancy. There are fewer cases in the first two months of pregnancy, but this is to be interpreted as a probable dis-

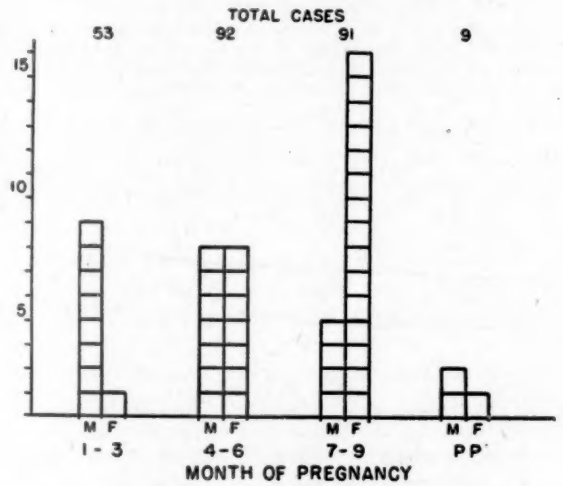

FIGURE 1. *Poliomyelitis in Pregnancy according to Month of Pregnancy and Sex of Child.*

crepancy in the data. I myself have missed a case in early pregnancy in a nurse in a Boston hospital, whom I thought to be unmarried. Of 42 of these cases in which both the month of pregnancy when the disease occurred and the sex of the child are known, there were 8 women with male infants and 1 woman with a female infant in the first trimester, equal numbers of infants of both sexes in the second and 15 women with female infants and only 4 with male infants in the third (Fig. 1). There were 3 cases that occurred post partum, — five, five and twenty-three days, respectively, — suggesting that infection was initiated during pregnancy.

Confirmation of this indicated localization of poliomyelitis in the first trimester in pregnancies with a male fetus, with a shift in the last trimester to a predominance in pregnancies with a female fetus, would establish a causal relation between pregnancy and poliomyelitis. In addition, it would afford a basis for the elucidation of physiologic or endocrine factors at different stages of pregnancy, that are involved in poliomyelitis. Furthermore, such a biphasic phenomenon may be a reflection of physiologic factors in pregnancy with a male or female fetus, a conjoint study with which might afford a clearer understanding of both susceptibility to poliomyelitis and factors related to sex ratio in pregnancy.

SUMMARY

Available statistics suggest that pregnancy predisposes to acute poliomyelitis and that there is a tendency for the disease to occur in the first trimester in women who are carrying a male fetus and in the third trimester in those who are carrying a female fetus.

It is hoped that additional data relative to these matters will be made available in the near future.

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CLINICAL NOTE

AN UNUSUAL CASE OF A FOREIGN BODY IN THE NECK*

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BOSTON

THIS report, which is extremely brief, is made chiefly because it presents an extraordinary traumatic episode. There is one lesson to be drawn from it that no member of this society needs to have told him.

A few years ago, in June, a group of children were playing on the wide and high piazza surrounding their house. Suddenly a boy of six lost his balance and tumbled head foremost from the piazza into a thick mass of rosebushes. He could not get up and moaned with pain, and his head was twisted at such an unusual angle that some of the others thought that his neck was broken. He was carried into the house, where the family physician saw him. The patient was sent to the local hospital, where I examined him. The rest of the case report follows.

Physical examination revealed a rugged boy lying on his back with his head sharply flexed to the left, a position from which it could not be moved. At the angle of the right jaw was a jagged, penetrating wound 2 cm. long, and lateral to it, under the skin and platysma muscle, could be felt the upper end of a thick, rodlike foreign body, which seemed to extend a long distance downward in the neck. if not into the thorax. The rest of the examination was negative. There was no significant evidence of shock.

It was at once decided that the penetrating object was probably a long stick and that an immediate attempt should be made to remove it.

Under ether anesthesia, a short, vertical incision was made over the most prominent part of the bulge, behind the penetrating wound. When the platysma muscle was severed, the rough, jagged end of a rose stalk protruded into the wound. A firm grip was obtained on it by means of a clamp, and gentle traction was started. There was an immediate massive hemorrhage from below, apparently of venous blood. The moment this happened the stalk was jammed back, and the bleeding at once ceased. The incision was carried almost to the upper border of the clavicle. When the contents of the carotid sheath had been dissected out, the stalk was found to penetrate completely the internal jugular vein and to extend behind the common carotid artery into the thoracic cavity. The jugular vein was carefully freed and tied with No. 1 chromic catgut above and below the point of penetration of the stalk. Before further traction on the stalk was attempted, the common carotid artery was dissected out as low down as possible and a double strand of No. 2 chromic catgut was placed around it, so that it could be pulled up quickly and tied. The stalk was then pulled up gently and there was no further bleeding. The patient was given 1500 units of tetanus antitoxin.

The patient's postoperative condition was excellent, and convalescence was without any untoward event.

When the stalk (Fig. 1) was laid on the boy's chest and neck, it extended from the wound of entrance down into the right thoracic cavity until the sharp end lay just behind the 4th rib.

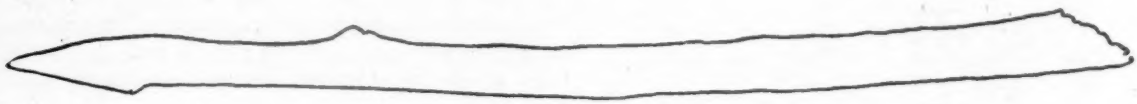

FIGURE 1. *Actual Tracing of the Stalk.*

The total length was 19.7 cm., with an average thickness of 0.8 cm. The blunt end of the stalk, seen at the right, was palpable just behind the angle of the jaw. The sharp end of the stalk penetrated the skin behind the angle of the jaw and went cleanly through the internal jugular vein, going down inside the thoracic cavity and stopping at the level of the fourth rib anteriorly.

It may seem to take a great stretch of the imagination to see how one can draw a direct and definite analogy between a surgeon's removing a foreign body of this sort from a child's neck and a collision at sea between two large vessels, but there is a direct one. It concerns the pushing of the rose stalk back into the neck and thorax. On September 18, 1914, the Canadian Pacific Steamship *Empress of Ireland* sank in the Saint Lawrence River with the loss of 1024 lives, having been rammed amidships by a Danish collier. The captain of the collier immediately reversed his engines and pulled his ship out, leaving the *Empress of Ireland* with a gaping hole, which made her sink almost immediately; if he had given the order "Full speed ahead," the vessels would have jammed together and the *Empress of Ireland* would probably have stayed afloat for some time.

264 Beacon Street

*Read by title at the postponed annual meeting of the New England Surgical Society, Boston, February 6, 1946.

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MEDICAL PROGRESS

DISEASES OF THE VEINS

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IN A previous review,[1] evidence by pathologists for the origin of venous thrombosis below the knees was presented. Serious illnesses, especially cardiac, injuries, operations and childbirth were proved to be the usual background for thrombosis, much of which was terminal and unnoticed clinically. The state of the blood platelets following childbirth and surgical operations was shown to predispose toward thrombosis, and patients might be more or less liable to it, as indicated by their tolerance for or sensitivity to heparin. Local conditions in the lower limbs, however, appeared to be more important factors than any others. Early ambulation did not by any means overcome such influences.

Pulmonary embolism, it was stated, was to be expected chiefly in patients over fifty years of age, but might occur in younger persons, even in those acquiring thrombosis in everyday life. It often imitated cardiac and pulmonary disease.

The distinction between an early, quiet, thrombosis (phlebothrombosis) and a late, obstructive thrombosis (thrombophlebitis) was brought out, as well as the various courses that any one lower-leg thrombosis might pursue, and the importance of this distinction was shown to lie in the necessity of applying the appropriate treatment to the different stages — vein interruptions being most appropriate for the early stage as a prevention of embolism.

Diagnosis of venous thrombosis was believed to depend not only on various local signs in the lower leg but also on an elevation of pulse rate and temperature as written on the clinical chart. Pulmonary embolism was shown to call attention to thrombosis oftener than any other single sign. The importance of electrocardiography in making the diagnosis was noted. Phlebography appeared to be regarded as a trustworthy diagnostic aid by some but not by others. Treatment of thromboembolic disease by anticoagulants and by surgical interruption of veins was discussed. The anticoagulants were gaining favor, particularly in the prevention of postoperative thrombosis, and most reports were devoted to this aspect of the subject. Little information was at hand regarding how long the treatment should be continued and how the break-off should be managed. Attempts to make the administration of heparin less expensive and more convenient than by the continuous intravenous method were described, these including the use of a menstruum from which slow absorption could take place.

Surgical treatment appeared to have become more or less standardized, division of the femoral vein being most frequently used, but a tendency was evident to perform some higher ligations, including that of the vena cava, to cope with high, advancing processes and obscure peripheral sources of embolism. In any event, bilateral disease was always to be considered. Suction of soft thrombus from the common femoral vein appeared necessary in many cases, but it was considered not altogether satisfactory and the question of combining anticoagulants with surgery was raised.

Finally, some notes were made on the frequency with which venous thrombosis might be associated with arterial embolisms and thromboses in the limbs, a tendency that might account for some pulmonary embolism in connection with amputation for arterial deficiency.

RECENT CONTRIBUTIONS TO THE THROMBOEMBOLIC PROBLEM

Subsequent contributions to the thromboembolic problem amplify and expand previous observations, without adding anything of a revolutionary nature.

Etiology

Hunter and his associates,[2] continuing their earlier studies, compare a second series with their first. They undertook to determine at autopsy the incidence of thrombosis in the femoral and adductor veins of the thigh and to learn, if possible, the effect of exercise on thrombus formation. Regarding recumbency as the greatest single factor in thrombus formation, and believing that phlebothrombosis might occur within two days after recumbency had been started, they found that in patients exercised systematically until shortly before death (from any cause), only 18 per cent exhibited thrombosis at autopsy, as opposed to 53 per cent when exercise was not employed. In respect to local, mechanical factors in the legs themselves, these authors quote from Simpson's[3] comment that pulmonary embolism was strikingly increased in elderly persons cared for in London bomb-proof shelters who reclined in deck chairs or something similar, the wooden crossbar causing pressure on the veins on the back of the leg and popliteal space.

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They believe that in hospitals all attendants should be embolism-conscious, particularly in respect to the lower legs as a source.

Hyperprothrombinemia, as a threat of thrombosis and embolism, is further discussed by Shapiro.[4] Observations were made on 59 cases in which present or recent thromboembolization was observed. Making use of a particular method of prothrombin estimation, Shapiro found that reactive hyperprothrombinemia could be detected by serial estimations after surgical operations, childbirth, acute coronary occlusion and some other disorders in a large proportion of cases. The detection of such a state could be used not only as an indication for treatment but also in the differential diagnosis between pulmonary infarction and other lesions presenting a similar symptomatology.

Venous pressures during various surgical operations have been studied by Davis, Gilman and Freedberg,[5] with the thought in mind that venospasm may play a part in the observed elevated pressures found.

That such vasoconstrictions and elevated pressures may lead to postoperative venous thrombosis is suggested but of course not proved.

Clinical Course

There is an evident tendency to belittle the distinction between phlebothrombosis and thrombophlebitis, except as they represent stages of the disorder. For example, Fine and Starr[6] encountered a soft detachable thrombus proximal to what seemed to be a typical thrombophlebitis. They declare that when embolism occurs in the presence of phlegmasia alba dolens it need not have come from the quiet, opposite leg but from the obstructed side. Thus, they recommend explorations, at an early or even an advanced stage of the acute swelling. This supports Allen, Linton and Donaldson's[7] view that in its early progress an obstructive thrombophlebitis is a proper subject for surgery. On the other hand, Ochsner,[8] in a complete discussion of intravenous clotting, holds the distinction between the stages to have clinical importance, not only because phlebothrombosis should be treated surgically but also because the various sorts of vascular spasm caused by thrombophlebitis, some of which may actually be contralateral, are most effectively treated by lumbar sympathetic block. Such matters will be reconsidered below under the heading "Treatment." They are mentioned here to show that the stages of the thrombosing process in the veins of the lower limbs *are* worthy of attention, and that if one concentrates so heavily on the embolic side of thrombosis as to ignore the distinction between the stages, one may fail to have in mind the serious reflex vascular constrictions, some of which have permanent disabling effects.

Diagnosis

Stress is laid on the value of early diagnosis, both by phlebography and physical signs. The value of the former is in controversy. Bauer[9] makes it a routine practice and pays great attention to the technic. He always cuts down on and cannulates the terminal trunk of the lesser saphenous vein below the external malleolus, declaring that its immediate deep connections, especially with the fibular (peroneal) veins, where much thrombosis originates, make it the ideal spot for the introduction of the contrast medium. Diodrast, or an equivalent iodine preparation, is used, and exposure to the x-ray from above the knee to the ankle is made with the limb in the horizontal position. This technic is believed to be decidedly more accurate than the insertion of a needle into any available superficial vein — diversion of the flow into the deep veins being forced by a rubber constriction about the upper calf — and probably accounts for Bauer's reliance on phlebography. Anderson and Patterson,[10] however, make use of the needle-and-tourniquet method and depend on phlebography to determine the type of treatment to be used in cases of chronic or recurrent venous thrombosis. They regard it as unnecessary as a preliminary to ligation in cases of acute or recurrent venous thrombosis when definite local clinical signs are present. Apparently Ochsner,[11] who once strongly favored phlebography, now relies on it much less than formerly.

Other refinements in early diagnosis are offered by Moses,[12] who explores the posterior calf for deep tenderness by firm pressure with the fingertips and follows the discovery of a tender spot by lateral pressure between the fingers and palm, and by Tyson and Goodlet,[13] who find that elevated venous pressure in the veins of the foot or ankle offers better evidence of thrombosis in the calf than can be secured by phlebography. Most observers look on slight enlargement, local deep tenderness and minor increases in the tone and irritability of the calf muscles, as ascertained by daily routine examinations, as most important. Spontaneous pain and pain on forced dorsiflexion of the foot are relatively late signs.

On the whole, little has been added lately to the diagnostic armamentarium, but if phlebography is to be used, the vein behind the external malleolus had better be exposed and cannulated. Consistent practice of this method in skilled hands will probably produce better results than any other one observation, the situation and extent of the process usually being revealed to the expert.

Pulmonary Embolism

The recent literature on pulmonary embolism adds a little to the understanding of both the path-

ologic physiology and the diagnosis. Attempts to study it experimentally have been made. Kinney, Haynes and Dexter[14] have introduced a venous catheter into the pulmonary artery in the dog by way of the jugular vein and right heart. So far, only the method has been described, but from an informal communication, as yet unpublished, I learn that occlusion of a large pulmonary artery, by the inflation of a balloon at the tip of the catheter, produces no change in the pulse rate or respiratory rate, the systemic blood pressure, the right ventricular pressure or the electrocardiogram. Only when infarction follows do signs and symptoms appear. If, however, emboli (lycopodium spores) are introduced into a lobe, acute symptoms, including a fall of blood pressure, dyspnea, elevated right ventricular pressure and acute electrocardiographic changes, at once occur. Apparently this reaction is due to a generalized constriction of the pulmonary arteriolar bed; that is, it is not confined to the affected lobe. Dexter and his associates are interested in the attempt to correlate these findings in human beings, and their observations should prove valuable.

Statistically, the thromboembolic problem is still being dealt with chiefly from the postoperative and post-traumatic viewpoint, although many of those most familiar with the subject evidently hesitate to rely on figures, even those secured from large clinics. Thus, Allen, Linton and Donaldson[7] comment that venous thrombosis is commoner in certain clinics and certain geographic locations than in others and that the age of the patient is of utmost importance in the consideration of the danger of fatal embolism in thromboembolic disease. They are so impressed with the increased danger from pulmonary embolism in the aged that they have begun to employ prophylactic vein ligation in prostatic patients, cancer subjects and even some cardiac patients of the older age groups. They find little danger of fatal embolism in patients under forty years of age.

As a result of a large experience in a Swedish hospital, Bauer and Jorpes[15] state that unless prophylactic and therapeutic measures are used to prevent it, thrombosis develops in 1 of every 60 patients who undergo operations or who receive other forms of treatment in surgical or medical wards, and 1 in every 5 or 6 patients who suffer thrombosis dies of pulmonary embolism. My comment is that the incidence of thrombosis given by these authors is extraordinarily low and their percentage of fatal embolisms rather high.

I consider that present-day statistics on both thrombosis and embolism merely emphasize the significance of the problem and that a study of the early signs of pulmonary embolism, together with an understanding of its nature and course, is of the greatest importance, both in medicine and in surgery.

The mode of production of pulmonary embolism has been interestingly discussed by Chapman and Linton.[16] Hitherto, they write, the emphasis on sudden death in the act of defecation, parturition, coition or lifting and straining at work or sports has been placed on changes in venous pressure and total hemodynamics due primarily to the heart itself. They explain so-called "bedpan" and similar deaths as due to a preliminary rise of venous pressure and blood volume in the lower limbs, by which the insecurely thrombosed veins are suddenly distended and pieces of thrombus are broken off; as pressure falls and the veins are emptied toward the heart, the embolus is washed along with the accumulated blood. Doubtless this explanation is true, but it should not be forgotten that patients suffering oppressive epigastric discomfort in the early stages of embolism may try for a bowel movement as a means of relief.

Pulmonary embolism from obscure sources is reported by Hampton, Prandoni and King.[17] Ten cases were observed, all of which were ambulatory and gave no history of phlebitis. The correct diagnosis was made only after considerable study. Dyspnea and chest pain were usually important clues. Probable sources of emboli were found in leg veins, pelvic veins, thrombosed hemorrhoidal veins and the plexus associated with the prostate. Anticoagulant therapy was successfully employed.

Surgical Treatment

The controversy between the advocates of ligation and of anticoagulants concerns not only the definitive treatment of thrombosis in the leg veins but also prophylaxis. I should preface the presentation of the two points of view by saying that all grant the value of maintaining muscular tone, exercising the legs and keeping up circulatory efficiency in patients forced into life in bed and by acknowledging that the advocates of early ambulation make no claim for the radical lessening of postoperative thrombosis by this means, some rather low figures (Blodgett and Beattie[18]) even suggesting that thrombosis is thereby increased.

The anticoagulants are represented by heparin and dicumarol and ligation mainly by bilateral ligation or section of the femoral vein, with the occasional employment of interruption of the iliac vein or vena cava.

I present first the operative surgical standpoint, which is represented most emphatically by Allen, Linton and Donaldson.[7] They believe in routine bilateral interruption of the femoral vein in the groin in all cases of thrombosis whether or not embolism has occurred, and in cases of early thrombophlebitis of the obstructive sort. Regarding the latter stage of the disease, they think that thrombectomy relieves the patient of many of the late complications that are well known to result from thrombophlebitis. They are begin-

ning to use bilateral section of the femoral vein in cardiac patients if an infarction has occurred or there are signs of thrombosis in the legs, but they have also made some prophylactic sections before any definite threat of embolism has presented itself. They have employed prophylactic ligation of the femoral vein in a small group of patients with fractures of the hip and in a good many prostatic patients. They believe that there is a definite future for prophylactic vein division, although they are not fully satisfied concerning the indications.

As regards the level of vein interruption, these authors like the idea of opening the superficial femoral vein distal to the profunda, although they make no special point of the exact level to be used. Their statistics, however, show that they have ligated the superficial femoral vein far oftener than the common vein, — in fact, in proportion of about four to one.

Fine and Starr[6] are equally surgically minded. They are strongly in favor of bilateral ligation and prefer the common femoral level for vein interruption, believing that any resulting edema is of minor consequence compared with the greater safety of section proximal to the profunda branches. They are opposed to any distinction between early thrombosis and thrombophebitis, for they think that embolism can occur in the presence of the latter, and they differ somewhat from Allen, Linton and Donaldson in making little distinction between the early and late stages of the obstructive, inflammatory disease. They speak favorably of ligations higher than the inguinal ligament as having less serious aftereffects than does ligation of the common femoral vein and say that such interruptions — of the common iliac vein or vena cava — seem to add no danger and result in fewer postoperative complications.

Veal and Hussey[19] throw an interesting light on the level of vein interruption in a series of 84 cases, in 39 of which embolism had preceded ligation. In the latter group 9 patients suffered further embolism after ligation. Of these 9 cases, embolism was believed to have occurred from the opposite or untreated side in 5, but in the other 4 the source of the embolus was the femoral vein above the point ligated. Veal and Hussey argue from these figures that surgery failed because of inadequate surgical treatment rather than because the principle of the treatment was faulty. In the other 45 cases, in which ligation was performed before the development of pulmonary embolism, there were no cases of embolism following the operation. My own experience supports Veal and Hussey's contention. Satisfactory as is ligation below (distal to) the profunda in many early cases, unexpected tragic embolisms have occurred from a point proximal to the interruption.

There are occasional reports of other disasters following vein ligation. Dennis[20] operated on a fifty-nine-year-old man for a rather acute, late thrombosis following a hernia operation. There had been considerable pain, pinkness and engorgement of the leg. The saphenous vein was thrombosed and palpable. The femoral vein was divided at the saphenofemoral junction and was found to be only incompletely obstructed. As a result of ligation of the vein, the leg at once became deeply engorged and distended with blood. Sympathetic blocks gave no relief. There was a good deal of shock, and the systolic blood pressure fell to 40. The administration of plasma brought no improvement. The leg was cold, tense and bluish-black. The deep fascia (aponeurosis) was divided from below the knee into the upper thigh on both sides of the leg, and the femoral artery was found to be pulsating normally. This operation relieved the violent, acute venous congestion, and both the leg and the patient's life were saved at the expense of considerable disability to the leg itself. My comment on this episode is that I have seen 2 cases of similar sort. In both, a large blood clot formed in the depth of the calf, both required extensive opening on the aponeurosis, and in both cases the clot became infected. Neither leg, however, was lost. Evidently, when the collateral vessels are already widely occupied by thrombus, interruption of the common femoral vein, as yet only partly obstructed, may trap an enormous amount of venous blood in the leg, resulting in both local and general circulatory damage — even shock.

Little is said by anyone about the obstinate edemas that occur following division of the common femoral vein, although Fine and Starr[6] allude to them and Allen, Linton and Donaldson[7] assert that they need not seriously be considered. It is my own belief that extremely careful supervision of the convalescence, with gradual resumption of exercise in the erect position, first without weight-bearing and later with it, especially if each course of exercises is balanced by a period of elevation of the legs in bed, will obviate most of the undesirable aftereffects. This is especially true in the unusual and perhaps unexpected cases of serious venous obstruction following ligation of the common femoral vein.

Ochsner,[8] whom I have already quoted as emphasizing the distinction between the various stages of thrombosis, believes in operations for phlebothrombosis, making use of lumbar sympathetic blocks for what he distinguishes as the inflammatory obstructive type causing reflex vasospasm.

De Takats and Fowler[21] reserve ligation of the femoral vein for such patients as have suffered a pulmonary infarction and show evidence of thrombosis in the calf. For these, they recommend ligation distal to the profunda. They regard ligation of the common femoral vein as a cause of chronic edema in some cases. They are, however, greatly interested in the use of heparin and dicumarol and, as has already been stated, make a point of studying the

reaction of the coagulation time to a test dose of heparin, believing that the patient's so-called "heparin tolerance" is of real clinical importance. Their discussion of the use of anticoagulants will be considered later under that heading.

The higher vein interruptions — that is, those above the common femoral vein — are of a good deal of interest. I[22] myself have advocated ligation or actual section of the common iliac vein for definitely unilateral processes — such, for instance, as occur in everyday life following minor trauma — and also for recurrent unilateral thrombosis. Interruption of the common iliac vein offers a vastly better collateral circulation than is available when the common femoral vein is ligated, especially in cases of fairly widespread thrombosis in the thigh without complete obstruction of the femoral vein itself. The difficulty with such operations is that in many chronic or recurrent processes both common iliac veins may be very friable and easily injured, that the left, for anatomical reasons, is often inaccessible and that a general anesthetic is required, as opposed to the local infiltration so satisfactory in the case of the femoral vein. It will be noted, however, that Fine and Starr[6] regard these operations as adding no appreciable risk. Bancroft[23] reports a satisfactory experience with them in a study of 12 cases in which sixteen thrombectomies were performed for thrombosis discovered at the operative level, but notes 1 death from embolism. All his operations were iliac explorations, and three were bilateral. He gave heparin by Loewe's method (see below) following operation and regards high vein sections as being on the whole safe and life-saving. Satisfactory as many operations on the common iliac vein have proved to be, they do not cover the problem of bilateral thrombosis, since separate incisions are required for the two sides and this seems a decidedly overcomplicated procedure when ligation of the vena cava can be performed at one stroke at only a little higher level.

Divisions of the vena cava have been employed in many cases when a bilateral process is present and appears to be uncontrollable or when the source of serious embolism is so obscure that one authoritative step to stop it must be taken. O'Neil[24] has had a highly satisfactory experience with these operations, regards them as exceedingly useful, has run into little danger in performing them and finds little disability afterward. He reports a considerable series of cases. A favorable account of ligation of the vena cava, with a history of the procedure, is offered by Northway and Buxton.[25] Still another report comes from Gaston and Folsom,[26] and Kern and Berman[27] record a successful division of the vena cava for a septic thrombosing process. It is unnecessary to emphasize that the approach to the vena cava offers difficulties not inherent in operations at a lower level. It is easy to reach the great vein through a lateral retroperitoneal incision, but the field offered by the unilateral exposure is so limited that if some of the delicate lateral veins entering the vena cava are torn, as by even the gentle pressure of a blunt ligature-carrier, it is extremely difficult to control the bleeding. Linton, in a personal communication, states that the best approach is by a right paramedial incision of considerable extent, pushing the peritoneum and the abdominal contents toward the left and obtaining a direct view of the vena cava and its branches from in front. Others have approached the vena cava transperitoneally. One must also realize that in some cases so enormous an amount of blood is trapped in the lower half of the body by sudden interruption of the vena cava that patients are occasionally thrown into serious or even fatal shock unless elevation of the legs is immediately and persistently employed.

Altogether, the operation has many times appeared to be life-saving but should not be undertaken by those not familiar with the difficulties of handling large blood vessels under a variety of circumstances.

This concludes the case for the surgical interruption of veins in the control of thrombosis and embolism. That for the anticoagulants is now to be presented. Special considerations, as in the case of fractures, will be taken up separately.

(*To be concluded*)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 32311

PRESENTATION OF CASE

A fifty-three-year-old man entered the hospital with jaundice.

For several years the patient had had slight postprandial gaseous indigestion produced by fatty foods; this was seldom troublesome, since he had been on a low-fat, low-protein diet because of gout of thirteen years' duration. He had taken colchicine during exacerbations of the disease, with great relief. One and a half years before admission he had the first attack of a colicky right-upper-quadrant pain, after which there was no further difficulty until six months before admission, when he had several episodes of similar pain. At that time a cholecystectomy was performed at another hospital. The gall bladder contained numerous stones. The common duct could not be identified. Postoperatively the patient became jaundiced and began draining large quantities of bile through a laterally placed stab wound. Six weeks later he was reexplored by another surgeon. Again the common duct could not be found. The portal vein was accidentally opened, and the patient lost a great deal of blood. Postoperatively bile drained through the wound, and the previous sinus closed. The jaundice disappeared. Subsequent to the first operation the stools had been acholic, but they turned brown after the second operation. Bile continued to drain until six weeks before admission, when the second sinus closed. Three weeks later the skin became mildly jaundiced and began to itch. Four days before admission there was pain in the right upper quadrant and in both shoulders. This was not related to respiration. During the following three days the patient vomited everything taken by mouth. He continued to have pain and passed scanty, dark urine. The stools were small and slate gray.

Physical examination showed moderate jaundice and slight diffuse tenderness in the right and left upper quadrants. The site of the previous sinus was extremely tender. There were diminished breath sounds and crackling inspiratory and expiratory rales at both lung bases.

The temperature was 97°F., the pulse 100, and the respirations 24. The blood pressure was 100 systolic, 60 diastolic.

The white-cell count was 22,300. The urine was dark amber and gave a + reaction for bile. X-ray films revealed linear bands of density at both lung bases. The upper lung fields were clear. The diaphragm was high on both sides. A film of the abdomen showed the common and hepatic bile ducts to be filled with gas (Fig. 1); no dilated loops of bowel were seen.

One hour after admission the patient began to have severe, agonizing left-upper-quadrant pain and quickly developed marked tenderness and spasm of the entire upper abdomen, particularly in the left upper quadrant. Peristalsis was high pitched and hyperactive, alternating with long periods of silence. He was writhing with pain when examined.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FIORINDO A. SIMEONE: I think it might be interesting to see the x-ray films first.

DR. JAMES R. LINGLEY: This is a film of the chest showing the high diaphragm on both sides, with linear bands of density at the bases consistent with atelectasis. This plain film of the abdomen shows a moderate quantity of gas in what looks like the colon, which does not appear to be appreciably dilated. This is the gas bubble of the stomach, and in the right upper quadrant it can be seen that the common bile duct, the hepatic duct and the radicles are completely filled with gas. There is no definite mass, and no evidence of stone.

DR. SIMEONE: I should like to discuss this case from the point of view of complications following the removal of a gall bladder for stones. The patient had postprandial gaseous indigestion produced by fatty foods, and a diagnosis of cholelithiasis was made, for which an operation was performed. He had gout of some twelve years' duration and took colchicine. I thought of the possible lesions associated with gout, but could not find any to account for the symptomatology before or after operation, nor could I find anything that suggested a toxic reaction to the occasional taking of colchicine during a few exacerbations of gout. The gout and colchicine may therefore be considered as purely incidental.

A year and a half before admission the patient had the first attack of colicky pain in the right upper quadrant, so that if this was gallstone colic he had his first attack at the age of fifty-one, which is perhaps slightly unusual but not too much so. Following that one attack he had no more trouble. If he had stones they were silent until six months before admission, when he had several episodes of similar colicky pain in the right upper quadrant, which probably appeared at frequent intervals, suggesting a stone in the common duct, although there is nothing in the record about nausea, vomiting, jaundice or chills and fever. Cholecystectomy was performed at another hospital, and the gall bladder was described as containing numerous stones. It

would be helpful if one knew, in addition to the number of stones, how large they were. Although at operation the common duct could not be found, presumably it was looked for, as indicated by the note that the common duct was not found. I am left with the impression that the stones were smaller than the caliber of the cystic duct, which led the surgeon to look for the common duct.

Postoperatively the patient became jaundiced and began draining large quantities of bile through a laterally placed stab wound. This, of course, brings up a problem that is generally feared in gall-

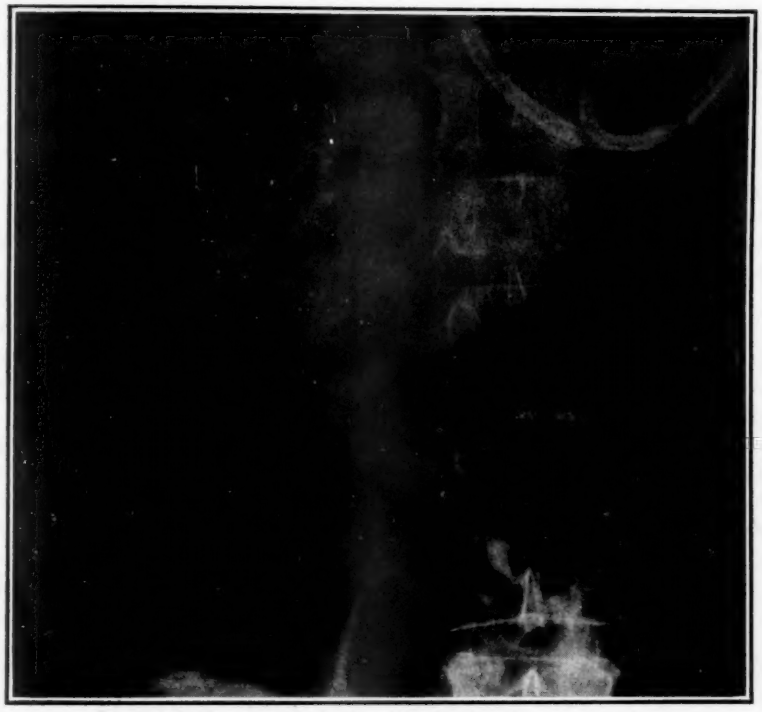

FIGURE 1. *Roentgenogram of Abdomen.*

bladder surgery, namely, injury to the common duct. In removal of the gall bladder the common duct is sometimes injured through outright carelessness; less often it is injured because of one of several anatomic anomalies of which the surgeon is not aware until too late. Although this is the first accident to suspect in this case, two points in the subsequent history make me doubt such a diagnosis. In the first place, the roentgenogram showed a common duct filled with air. Secondly, jaundice disappeared and bile appeared in the stools, suggesting that the common duct re-established continuity with the duodenum or other part of the bowel spontaneously after the second operation, which was done because of the jaundice and because of the persistent bile-draining sinus six weeks after the first operation. Again, the common duct could not be found. Perhaps the stricture had been resected or was anomalous and therefore difficult to recognize, or was located in densely scarred gastrohepatic omentum and difficult to dissect and identify. At the second operation the portal vein was accidentally opened, and the patient lost a great deal of blood. We are not told what happened at the second operation, but I imagine that little more was done after the puncture of the portal vein. I suspect that the accident occurred early in the operation, probably before the surgeon had a chance to mobilize the duodenum to identify the common duct transduodenally; this procedure might have favored the establishment of a fistula between the bile ducts and duodenum. It is difficult to understand how the surgeon opened the portal vein without encountering the common duct, because of the anatomic relations of the two structures.

Postoperatively bile drained through the wound, the persistent sinus eventually closed, and the jaundice apparently disappeared, because a new external fistula was formed from the common duct, or perhaps the old fistula was cut across and drained through the wound. The stools turned brown after the second operation, however, so that bile must have been getting into the intestines. I should like to explain that on the basis that at the time of the first cholecystectomy the patient probably had a stone in the common duct as well, which did not cause jaundice until after the operation and somehow became dislodged temporarily after the second

operation. Stones in the common duct are not an unusual finding in cholelithiasis. In 1940 Allen and Wallace[1] reported that in a series of 860 cases in this hospital during a four-year period roughly 1 out of 5 patients with cholelithiasis had stones in the common duct and that in almost half (46.8 per cent) the cases in which the common duct was explored, stones were found. It is therefore not unlikely that this patient with numerous stones in the gall bladder had a stone in the common duct, which was not found at the first operation.

Bile continued to drain until six weeks before he was admitted to this hospital, where the second sinus closed. Three weeks before admission the skin became mildly jaundiced and itched. For three weeks, then, the patient had no external biliary fistula and no jaundice. Four days before admission there was pain in the right upper quadrant and in both shoulders. This was not related to respiration. For the next three days the patient vomited everything that he took by mouth. That could have been due to recurrent common-duct obstruction from stone or a leak through the old biliary sinus, and a subhepatic abscess, with pressure on the duodenum, might have formed. He continued to have pain and passed brown stools. Apparently bile was still reaching the intestine.

The diminished breath sounds and crackling inspiratory rales are accounted for by the elevated diaphragm, which resulted from inflammation beneath it and which caused atelectasis in both lower lobes. Physical examination showed diffuse tenderness in the right and left upper quadrants, suggesting an inflammatory lesion in the upper abdomen, but the temperature was recorded as 97°F.; so that unless this man was in extremis as a result of the infection, he was not showing the expected temperature rise, which may be taken as evidence against a subhepatic abscess. The pulse was rapid, and the blood pressure low. These findings, along with the low temperature, suggest several possibilities. Perforation of a malignant or benign lesion of the stomach is unlikely. The roentgenogram of the abdomen did not suggest mechanical intestinal obstruction, which should be considered because special mention is made of intermittent high-pitched peristalsis. The history is consistent with mesenteric thrombosis, but again there was no x-ray evidence of intestinal obstruction. The temperature, white-cell count and blood pressure are consistent with mesenteric thrombosis or with acute pancreatitis. The history of repeated abdominal operations, with some inevitable infection, favors the former; the jaundice and cholelithiasis and the suspicion of choledocholithiasis favor the latter.

If the presence of an intact common duct is accepted, the x-ray finding of gas in the biliary tree is difficult to explain. The most plausible explanation for such gas is a fistula between the bile ducts and the duodenum. No evidence of injury to the duodenum, which might have favored the establishment of such a communication, was found, and no mention is made of digestion of the skin about the draining sinuses. In rare cases, gas regurgitates into the biliary tree through the papilla of Vater.[2] In one case these ducts filled with barium during an examination of the stomach for carcinoma, which made me think that the final episode was a perforation of a cancer of the stomach, but there is nothing in the history to indicate such a diagnosis. Cases have been encountered with regurgitation of air and injected barium through the papilla of Vater when a stone has been impacted in the papilla.[2] I should like to explain the course of events in this patient on that basis. The acute episode of severe agonizing left-upper-quadrant pain could have been due to acute pancreatitis secondary to stone in the ampulla. My final diagnosis is therefore residual stone in the common duct, with acute pancreatitis.

DR. EDWARD B. BENEDICT: How about a stone in the pancreatic duct?

DR. SIMEONE: I do not believe that that would produce jaundice unless it were close to the junction with the common duct.

DR. BENEDICT: I mean in addition to the pancreatitis. Such stones are often demonstrated by x-ray.

DR. TRACY B. MALLORY: Does one ever have pain with stone in the pancreatic duct? There is no muscle in the duct, and I do not see how it could go into spasm.

DR. SIMEONE: Cases with calcification have been reported in the head and body of the pancreas, with excruciating pain, which is relieved by subtotal pancreatectomy.

DR. MALLORY: Pancreatitis would offer a good explanation of the pain, but I doubt that colic can arise from the pancreatic duct.

DR. LINGLEY: I do not believe that we have seen gas in the common duct with cancer of the ampulla. Is it not rare?

DR. SIMEONE: I think that 5 or 6 cases are reported in the literature with gas in the biliary tree in the presence of an intact common duct and papilla of Vater.

DR. LINGLEY: Unfortunately, the cases that we have seen have been due to fistula between the duct and the bowel.

DR. CLAUDE E. WELCH: A number of considerations that Dr. Simeone has not mentioned troubled me. If I can interpolate a few facts into the history, this may be made clearer. In the first place, there was no question in the mind of the doctor who referred the patient to us that his patient had had an injury of the common duct. Ever since Dr. Allen[3] published his method for the surgical repair of injuries of the duct, we have been confronted with many of these cases. In the case under discussion, at the time of the second operation, the surgeon

tried to repair the duct, but in attempting to make the exposure the portal vein was entered and the operation had to be terminated after a stormy time on the operating table. The patient gradually recovered, and was finally slated to come to this hospital for repair at an optimum time. The surgeon called, however, and said that if the patient did not get into the hospital within three or four days, he would be dead at home. Consequently, he entered the hospital as an emergency case and was rather ill when first examined. A few hours after entry, having been previously quite comfortable, he began to have severe, agonizing, colicky abdominal pain, with high-pitched peristalsis. An x-ray plate was made, and the report that we received was that there was gas in the liver radicles and also dilated loops of small and large bowel. The radiologist in charge that night thought that this represented intestinal obstruction. The gas in the biliary tract, we thought, probably entered from a spontaneous fistula into the duodenum, although the possibility of a transverse-colon fistula had to be considered. Since the pain was colicky and because of the dilated loops of bowel and the fact that the abdomen quickly became tender throughout, we thought it most probable that he had developed a strangulating obstruction, although as a second possibility imminent perforation of an abscess through the liver into the peritoneal cavity near the common duct was considered.

A right-upper-quadrant incision was made. No evidence of intestinal obstruction could be demonstrated. On coming down to the region of the foramen of Winslow we found pus that had a foul odor, indicating that an abscess was perforating at this point. We assumed that it was coming from the liver or from the common duct. We were able to open into the hepatic bed and, finding the stump of the common duct, to insert a T tube into the common duct and into the viscus that was adherent at the portal fissure. The patient's condition was poor at operation. He drained bile for twenty-four hours freely through the tube. The bile was followed by pus and then by fecal drainage. He never really improved, and died almost on the same schedule as his doctor had predicted.

Clinical Diagnoses

Small-bowel obstruction.
Choledochojejunal fistula.
Obstructive jaundice.
Pulmonary atelectasis.

Dr. Simeone's Diagnoses

Residual stone in common duct.
Acute pancreatitis.

Anatomical Diagnoses

Benign stricture of common bile duct.
Choledochoduodenocolic fistula.
Multiple abscesses, hepatic, subhepatic and diaphragmatic.
Acute fibrinopurulent pericarditis.

Pathological Discussion

Dr. Tracy B. Mallory: Autopsy showed a complicated picture. There was a double fistula from the remnants of the common duct; one went into the duodenum, and the other into the hepatic flexure of the colon. There were two benign strictures in the common duct, one above and one below the area of the fistulas. There was also a communication into a hole in the liver, which was probably an abscess cavity, and led to the left hepatic duct. A small old abscess was found in the region of the head of the gall bladder. There were dilatation of all the intrahepatic bile radicles, multiple abscesses throughout the liver and a considerable subhepatic abscess. Infection had extended into the diaphragm, which was split into two leaves by a collection of pus. There was also acute fibrinopurulent pericarditis. We could not find persisting stones anywhere, and the pancreas — surprisingly enough, in the face of all this biliary infection — showed no trace of inflammation.

Dr. Benedict: I do not see how the agonizing left-upper-quadrant pain is explained.

Dr. Welch: I thought that was explained at the time of the autopsy, because in dissecting between the leaves of the diaphragm we found this great abscess, which must have contained 500 cc. of pus. The pus was entirely above the peritoneum and was not in the pleura. It finally perforated into the pericardium.

References

1. Allen, A. W., and Wallace, R. H. Surgical management of stone in common bile duct: follow-up studies with special reference to graded dilatation of sphincter of Oddi. *Ann. Surg.* **111**:838-847, 1940.
2. Davis, L. Reflux of duodenal contents through common bile duct. *New Eng. J. Med.* **200**:313-320, 1929.
3. Allen, A. W. Method of re-establishing continuity between bile ducts and gastro-intestinal tract. *Ann. Surg.* **121**:412-424, 1945.

CASE 32312

Presentation of Case

A fifty-nine-year-old housewife entered the hospital complaining of pain in the epigastrium.

Five years before admission the patient, who had previously had fair digestion and no abdominal pain, suffered a severe hematemesis. Thereafter there was almost continuous epigastric discomfort. When she worked too hard or stretched, pain developed in the upper abdomen. There was no further vomiting or passage of black stools after the original episode. One month before admission a severe mid-epigastric pain doubled the patient and required morphine for relief. It radiated slightly to both sides. From then on she had continuous nagging pain, without other symptoms. During this period

the patient had been on a Sippy regime. There was a recent weight loss of 9 pounds from her normal weight of 107 pounds. Numerous x-ray films were taken during her illness, including a gastrointestinal series six months and a chest film two weeks before admission, which were said to be negative. Because it was thought to emanate from the spine the pain was treated by a back brace. She had had slight low-back pain, attributed to rheumatic changes shown in x-ray films of the spine. There had been no jaundice or acholic stools, constipation, diarrhea or distention.

The past history was not remarkable, except for the implantation of radium per vagina for menorrhagia at the menopause, thirteen years before admission.

On physical examination there was a firm, nontender mass in the epigastrium, which moved with respiration and transmitted a powerful aortic pulse. Both kidneys were palpable.

The temperature was 98.0°F., the pulse 70, and the respirations 18. The blood pressure was 160 systolic, 90 diastolic.

The hemoglobin was 10.2 gm. per 100 cc. of blood. The white-cell count was 10,600. The urine was normal. The stool was light brown and gave a negative guaiac reaction. X-ray studies revealed a crater, 3.0 by 2.5 by 2.0 cm., in the posterior wall and lesser curvature of the stomach just below the cardia. It appeared to be in a filling defect, the upper margin of which was somewhat shelf-like. The remainder of the stomach showed rather small peristaltic waves, without definite evidence of rigidity except for an area about 3.0 cm. below the lower margin of the lesion. The duodenum and the rest of the intestine were normal. One hundred cubic centimeters of fluid aspirated from the fasting stomach contained 3 units of free hydrochloric acid per cubic centimeter; there was no free hydrochloric acid in the 8-cc. specimen after alcohol. An electrocardiogram was normal.

A gastroscopy was done on the tenth day. The instrument was blocked at the cardiac orifice, but it was possible to see beyond the obstruction to the lesser curve, where a 3-cm. ulcer was visible on the anterior wall. It had slightly irregular margins and a sloughed base.

Operation was performed on the twenty-sixth hospital day.

Differential Diagnosis

Dr. Milford D. Schulz: This is the story of a patient presenting a complaint of abdominal discomfort and pain of which she had not been entirely free for five years. The first episode was accompanied by hematemesis, which was not repeated. She had received treatment intended to control a peptic ulcer, although there had never been visible evidence of a gastric or duodenal lesion until after the acute episode a month before admission, when further study of the upper gastrointestinal tract with the help of a roentgenologist and an endoscopist demonstrated a large ulcerating lesion high on the stomach wall. The variance of opinion regarding whether the lesion was on the anterior or posterior wall is understandable when one considers the problems of orientation in this area.

This problem resolves itself into the differential consideration of ulcerating lesions of the stomach.

Since I should like to discuss this case mainly from the standpoint of a roentgenologist, a review of the x-ray findings might be helpful. The ulcer, which was 3 cm. in size, was unusually high and although not on — but toward — the lesser curvature, it seemed in fact to be above the lesser curvature and in the fundus. The ulcer did not appear to protrude beyond the stomach entirely but rather to lie intraluminally as though in a mass about which a so-called "shelf" was described. This was probably the fluoroscopist's observation and is most important. It is certainly not an observation, however, that cannot be wrong, for the fundus is sometimes difficult to examine satisfactorily. No abnormality of peristalsis was demonstrated, although some rigidity was described just below the crater. Again, when the lesion is beyond the reach of the palpating hand, this observation is uncertain. The mucosal pattern did not seem to be altered, except in the immediate vicinity of the crater, where the appearance of convergence of folds toward the ulcer may have been merely apparent, owing to the projection of the fundus. No soft-tissue mass outside the projected wall of the stomach was demonstrated.

Tumors of the spindle-cell variety may be benign or malignant, are slowly growing and often ulcerate, sometimes quite early, leading to abrupt and intermittent bleeding, which may be the only presenting complaint. The history in this case is not incompatible with such an occurrence. But these tumors lie in the wall of the stomach and grow submucosally, more or less equally in all directions, stretching and bulging the stomach wall into a smooth crescentic defect over which the folds of an intact mucosa are smoothed out except where the usually somewhat centrally placed ulcer extends into the large, rounded soft-tissue mass outside the wall of the stomach, which can occasionally be seen on adequate x-ray films. A spindle-cell tumor is suggested by the long history, with early and noncontinuous bleeding, by the palpable mass, and by the recent episode after which a previously undiscovered ulcer was found, which may have meant recent ulceration; furthermore, an unulcerated extramucosal spindle-cell tumor in this position can easily be overlooked. Since none of the characteristic x-ray findings were present in this case, I shall dismiss this diagnosis. It might still be entertained, however, as an outside chance.

Hodgkin's disease, lymphoblastoma and lymphosarcoma may cause infiltration, with subsequent ulceration of the stomach wall, and it is frequently quite impossible to do more than suspect that a given lesion may be on this basis. But characteristically the picture is that of a rather plastic stomach wall, with overlying, thick and rigid mucosal folds within which the ulceration may be present. Such a lesion does not seem likely.

Areas of ulceration infrequently occurring in gastritis are usually small and multiple, and the findings of gastritis predominant.

Among the granulomas of the stomach in which ulceration occurs, syphilis is most frequently thought of and only rarely seen, as in ulceration in the thickened, stiff and shrunken stomach wall of a so-called "leather-bottle stomach." Ulceration of a gummatous lesion in the stomach is still rarer — enough to be thought of only when nothing else seems to fit the diagnosis and when the serologic findings are indicative. More rarely still has ulceration in the stomach, said to be on an acid-fast basis, been described in a patient with pulmonary tuberculosis. In the case under discussion the serologic findings were apparently not incriminating, and the chest was certainly not.

Neoplasms arising outside the stomach that have become adherent to it occasionally cause ulceration of the mucosa, most frequently, perhaps, cancer of the colon, but nothing in this case suggests anything amiss in the colon. Tumors of the pancreas or other abdominal tumors, such as lymphoma, also cause ulceration. The gastric diverticulums that are occasionally seen in the fundus of the stomach should not be mistaken for significant lesions.

This leaves to be considered the two most frequent causes of ulceration of the gastric mucosa: benign ulceration of the stomach and an ulcer due to a cancer of the stomach. The old problem concerning the relation of cancer to pre-existing ulcer will not be discussed. I should like to mention what I think is the real burden of this presentation. I do not want to be an apologist, but it seems well to point out the limitation of the roentgenologist in determining in every case whether or not an ulcer is benign. The limitations are much the same as those imposed on the surgeon when he has the abdomen open and the viscus exposed and on the pathologist when he has only the gross specimen, with the added drawback of his inability to observe small metastases to the liver and regional lymph nodes. Usually the differentiation is quite reliable. There are findings that suggest a malignant lesion, and others that are either equivocal or difficult to assay. As a rule it is easier to say that a lesion is malignant than that it is not. Demonstration of malignant changes have often to await detailed histologic study.

Characteristically a benign ulcer lies on or close to the lesser curvature, but many ulcers in this position have proved to be malignant and others located elsewhere in positions often thought to be unusual for benign ulcers have proved to be nonmalignant The last three simple ulcers on the greater curvature seen in this hospital were benign. The high incidence of malignant changes in prepyloric ulcers is well known. The size of an ulcer is not a reliable criterion; neither is roughness or smoothness of the base. Irregularity may be due to tumor granulations or food particles. The duration of the disease is also not diagnostic. The course of an ulcer under active management may be helpful: if it heals and leaves no rigidity of the wall, it is quite likely to be benign, but an ulceration in a tumor that heals or fills with tumor or food usually leaves stiffening behind, which represents tumor infiltration. Perhaps the most reliable sign denoting ulceration in a tumor is the actual demonstration of the tumor in which the ulcer lies. A benign ulcer lies or projects beyond the wall of the stomach — the other lies within the projected wall of the stomach intraluminally, giving rise to the so-called "meniscus sign of Carmen." This is not infallible, however. A large inflammatory reactive mass may be mistaken for tumor, or an ulcer in a tumor may penetrate deeply, and the finding is not always easy to demonstrate with complete satisfaction.

Rigidity of the stomach wall about an ulcer such as that in the case under discussion is most frequently, but not always, due to infiltration by tumor, as is also gross deformity of the gastric mucosal folds about an ulcer.

In this case one would like to speculate on the likelihood of a gastric ulcer, atypical in location and for this reason long overlooked, that had recently perforated — possibly into the liver, which lies in contact with this part of the stomach. This could have resulted in the formation of a large inflammatory mass, which was the palpable tumor and which might have been mistaken for the mass about the visualized ulcer. The location was unusual, however, and the ulcer was large, and rigidity of the wall was described. And there was a mass that presented a shelf-like defect — an intraluminal tumor in which the ulcer was situated. And since no subsequent examination demonstrated this to be a faulty observation, it must be accepted.

The diagnosis of leiomyosarcoma still intrigues me, in spite of the fact that the x-ray findings are not typical. The story is not inconsistent with cancer of the stomach, which is by far the most frequent tumor. The x-ray findings gave evidence of some kind of tumor. This all leads to a diagnosis — admittedly based largely on a single examination — of ulceration in a cancer of the fundus. The safest thing, of course, would be to say an ulcerating lesion of the stomach that was not conclusively benign.

DR. EDWARD B. BENEDICT: The gastroscope met with complete obstruction at the cardiac orifice. That usually means a carcinoma, but in a case of ulcer high up close to the cardia with spasm, the gastroscope may meet with complete obstruction. The ulcer itself looked irregular, in spite of a smooth margin. That observation has been slightly in favor of cancer, although severe gastritis around an ulcer may produce a similar effect. I thought from the gastroscopic standpoint that the ulcer was probably malignant, although the five-year history seemed rather long. It seems to me in any of these cases that the important thing to decide is not whether or not the lesion is benign but whether or not to operate. I should rather operate on a benign ulcer erroneously than to let a malignant ulcer go without operation. The decision was therefore made to operate on this patient.

CLINICAL DIAGNOSIS

Carcinoma of stomach?
Gastric ulcer?

DR. SCHULZ'S DIAGNOSIS

Ulcer in cancer of stomach.

ANATOMICAL DIAGNOSIS

Benign peptic ulcer.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was operated on by Dr. Richard H. Sweet via the transthoracic route, which is obviously indicated with a lesion as high in the cardia as this one was. He found a very indurated mass in the stomach, which was densely adherent to the pancreas. He carefully searched the abdominal cavity but found no evidence of metastases. He was still uncertain whether the lesion was benign or malignant, but believed that it was readily resectable and proceeded with the operation. The only difficulty met with was in dissecting it free from the pancreas. The microscopic sections showed a benign peptic ulcer, with no evidence of neoplasm.

The unusual points in the case have been brought out by Dr. Schulz: this lesion was much higher in the stomach than benign ulcers are usually found, and the area of ulceration was considerably larger than that ordinarily seen with benign ulcers. There is essentially no limit to which a benign ulcer can reach, however. I have seen one 10 cm. in diameter, three times as large as the one in the case under discussion.

lishment: *Provided*, that such person is supplied with a written statement from the patient's physician or, in the case of an establishment engaged in the care and treatment of the sick, from a responsible official thereof who is a practicing physician, and such written statement shall be valid for a period of not to exceed sixty days from the date of issuance and shall specify (i) The milk fat content of cream required for such use, (ii) the daily quantity of such cream, and (iii) with regard to the necessity of such cream for supervised medical treatment: *Provided further*, that such written statement shall not be valid for obtaining such cream unless approved by a public health officer who is a physician, or by the secretary of the county medical society of the county wherein such patient resides or such establishment is located.

2. Upon application by one or more persons in any area or region and after demonstration to the satisfaction of the Administrator that compliance with the provisions of (b) (1) hereof will not tend to conserve milk fat for defense and essential civilian needs, or upon the initiative of the Administrator, the Administrator may grant an exemption from the provisions of (b) (1) hereof to any or all persons in such area or region specified by the Administrator.

Finally, any person who feels aggrieved by this regulation may file a petition for relief with the War Food Order Administration and send his or her communication to the War Food Order, No. 149, Dairy Branch, Production and Marketing Administration, United States Department of Agriculture, Washington 25, D. C.

MICHAEL A. TIGHE, M.D., *Secretary*

DEATHS

CHANDLER — Harold B. Chandler, M.D., of West Newton, died July 14. He was in his sixty-first year.

Dr. Chandler received his degree from Harvard Medical School in 1911 and had limited his practice to ophthalmology.

His widow, two daughters and a son survive.

ELLMS — Evelyn B. Ellms, M.D., of Waban, died July 14. She was in her fortieth year.

Dr. Ellms received her degree from Tufts College Medical School in 1932. She served as a lieutenant in the Navy Medical Corps during World War II and was a fellow of the American Medical Association.

Her mother and a brother survive.

CORRESPONDENCE

RESIDENCY TRAINING IN MASSACHUSETTS VETERANS ADMINISTRATION HOSPITALS

To the Editor: The establishment of a Department of Medicine and Surgery in the Veterans Administration, as provided for under Public Law 293, has led to the development of an extensive residency training program in many Veterans Administration hospitals. It is hoped that this program will result in securing for the veteran patient a standard of medical and surgical care comparable with that rendered in the best civilian hospitals. To secure the best advice and assistance in carrying out such a program, the Veterans Administration has called on the deans of schools of medicine to give counsel in all matters pertaining to the education and training of residents and is, with the help and advice of the deans, appointing qualified staffs of part-time civilian specialists. These specialists will carry on much of the residency training.

The Deans' Committee for the Massachusetts Veterans Hospitals consists of Dean Dwight O'Hara of Tufts College Medical School, chairman, Dean C. Sidney Burwell of Harvard Medical School, Dean Donald G. Anderson of Boston University School of Medicine and Dr. Dale Friend, of Harvard Medical School, secretary. Each dean has selected two advisors; one in medicine and one in surgery. These advisors are Drs. Laurence B. Ellis, James M. Faulkner, Roger C. Graves, Chester S. Keefer, Reginald H. Smithwick and Augustus Thorndike.

Part-time civilian specialists are divided into two categories depending on the degree of experience and skill, teaching qualifications and need. The first group consists of senior physicians of outstanding ability — those of professorial caliber in the medical schools or of equivalent standing among the practicing profession of the community. These men are called consultants. They assist and advise the chief of the service in the veterans hospital concerning organization, care of patients and appointment of residents and take a prominent role in the teaching of residents by ward rounds, seminars, clinics and demonstrations. They are also available to the hospital for consultation in all matters relating to their specialities as applied to the care and treatment of patients. It is desirable that consultants be certified by their specialty board and be veterans of either World War I or World War II. They must be approved by the Deans' Committee. The number of visits is regulated by the needs of the particular hospitals. The second group consists of younger physicians of proved ability who are members of medical-school staffs or have an equivalent standing in the practicing profession of the community. These men are called attendings. They actively participate in the care of patients by conducting ward rounds, performing operations and carrying out such other therapeutic measures as may be required. They also assist and advise in the organization of services and take a prominent role in teaching residents. The chief of the service delegates much of the care of the patients to these men. The Veterans Administration, of course, is responsible for the care and treatment of patients, but the chief of service, as the representative of the Veterans Administration, delegates responsibilities according to the merits of the case. The attendings participate in clinics, seminars and demonstrations and assume a great deal of the teaching load. They must be certified by their specialty board, be veterans of World War II and be approved by the Deans' Committee. The number of visits vary according to the needs of the hospitals.

Physicians accepted for residency training must be graduates from approved medical schools and veterans of World War II, must have the intention and ability to go on to specialty-board certification and must be approved by the Deans' Committee.

The Veterans Administration hospitals at present interested in the residency training program are those located in Bedford, Rutland Heights and West Roxbury. The West Roxbury Hospital has been actively studied by the Deans' Committee, and a qualified staff has already been appointed. It is anticipated in the near future that this hospital will have the approval of the various specialty boards as a suitable institution for residency training. The newly appointed staff consists of the following physicians:

CONSULTANTS

Dr. C. H. Allman	Ear, nose and throat
Dr. J. C. Aub	Endocrinology
Dr. T. L. Badger	Chest diseases
Dr. J. S. Barr	Orthopedic surgery
Dr. H. K. Beecher	Anesthesia
Dr. W. M. Daland	Plastic surgery
Dr. W. Dameshek	Hematology
Dr. J. G. Downing	Dermatology
Dr. J. Homans	Vascular surgery
Dr. T. Lanman	Surgery
Dr. J. R. Lingley	Roentgenology
Dr. W. A. Meissner	Pathology
Dr. L. Parsons	Gynecology
Dr. F. Rackemann	Allergy
Dr. B. Sachs	Ophthalmology
Dr. G. C. Shattuck	Tropical medicine
Dr. R. Stetson	Medicine
Dr. M. Strock	Maxillofacial surgery
Dr. G. Taylor	Surgery of tumors
Dr. R. G. Vinal	Rehabilitation
Dr. S. N. Vose	Urology
Dr. C. Wesselhoeft	Communicable diseases
Dr. P. White	Cardiology

ATTENDINGS

Dr. D. Adams	Medicine
Dr. B. Banks	Medicine
Dr. N. J. Bakst	Medicine
Dr. R. H. Betts	Thoracic surgery
Dr. W. Bloomberg	Neuropsychiatry
Dr. T. Botsford	Surgery
Dr. W. Buddington	Urology
Dr. R. Chute	Urology
Dr. J. Drooker	Ear, nose and throat

Dr. W. Elliston	Orthopedic surgery
Dr. J. E. Flynn	Surgery
Dr. J. Frazee	Ear, nose and throat
Dr. I. H. Jaffee	Medicine
Dr. K. B. Lawrence	Surgery
Dr. W. F. Leadbetter	Urology
Dr. E. H. Lewis	Anesthesia
Dr. J. Messina	Dermatology
Dr. L. Pilcher	Surgery
Dr. L. Soutter	Surgery
Dr. J. Stillman	Medicine
Dr. G. L. Sullivan	Ophthalmology
Dr. A. Thibodeau	Orthopedic surgery
Dr. T. Urmy	Medicine
Dr. J. Townsend	Medicine
Dr. W. R. Wegner	Neurosurgery

RESIDENTS

Dr. D. V. Baker	Surgery
Dr. W. J. Baker	Surgery
Dr. V. B. Ballard	Medicine
Dr. R. E. Barkin	Medicine
Dr. C. D. Belcher	Surgery
Dr. M. Blum	Medicine
Dr. J. S. Chambers	Surgery
Dr. H. R. Clement	Medicine
Dr. J. F. Cooper	Surgery
Dr. R. Evans	Medicine
Dr. A. Finck	Surgery
Dr. D. Freni	Surgery
Dr. R. Grissom	Surgery
Dr. J. W. Hattshorn	Surgery
Dr. G. V. Levreault	Medicine
Dr. S. Levine	Medicine
Dr. S. Manelian	Orthopedic surgery
Dr. R. L. Ohler	Medicine
Dr. M. H. Rose	Medicine
Dr. L. Ryack	Medicine
Dr. R. Vaughn	Surgery
Dr. G. Warren	Urology
Dr. A. S. Zdanis	Medicine

In addition to the above appointments the following physicians have accepted full-time positions in the Veterans Administration and have been assigned to the West Roxbury Hospital:

Dr. John Houghton	Chief of pathology
Dr. D. Littman	Cardiology
Dr. John Poutas	Clinical director
Dr. J. L. Rudd	Physical medicine and rehabilitation
Dr. Samuel Tartakoff	Chief of neuropsychiatry
Dr. Richard Warren	Chief of surgery
Dr. Thomas Warthin	Chief of medicine
Dr. Egon Wissing	Chief of roentgenology

Preliminary studies have been made of the needs of the Neuropsychiatric Hospital at Bedford. The Neuropsychiatric Subcommittee, consisting of Dr. Harry Solomon, of Harvard Medical School, chairman, Dr. William Malamud, of Boston University School of Medicine, and Dr. Clifton Perkins, State Commissioner of Mental Diseases, is at present formulating plans for training at Bedford. The following part-time physicians have been appointed to the staff at Bedford: Dr. Douglas Thom, consultant in neuropsychiatry; Dr. Sylvester B. Kelley, consultant in urology; and Dr. Jackson Thomas, attending in neuropsychiatry. Dr. Norman Elton is chief of pathology and a full-time Veterans Administration appointee. As the needs are more fully ascertained, more part-time appointments will be made and residents will be assigned.

The tuberculosis hospital at Rutland Heights is also under study. Up to the present time little change has been made other than the appointment of Dr. L. Davenport as consultant in chest diseases and of Dr. D. Harken as consultant in thoracic surgery.

The Cushing General Army Hospital at Framingham will be taken over by the Veterans Administration on October 1, 1946. The program that has been carried out at the West Roxbury Hospital will be put into effect. It is anticipated that this hospital will have 1000 beds, which will provide many openings for consultants, attendings and residents.

The Dean's Committee is happy to report that it has had excellent co-operation from the Veterans Administration and from the physicians of the region. There is every reason to believe that this program will, as it develops, ensure that the veteran will receive the best available quality of medical care and that it will also provide an excellent opportunity for residency training leading to certification by the various specialty boards.

DALE FRIEND, *Secretary*

Harvard Medical School
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Psychology of Women: A psychoanalytic interpretation. Volume II: *Motherhood.* By Helene Deutsch, M.D., associate psychiatrist, Massachusetts General Hospital, and lecturer, Boston Psychoanalytic Institute. 8°, cloth, 498 pp. New York: Grune and Stratton, 1945. $4.50.

In this second volume Dr. Deutsch has completed her work on the psychologic life of the normal woman and discusses all the aspects of motherhood.

Local Health Units for the Nation: A report. By Haven Emerson, M.D. With the collaboration of Martha Lubinbuhl, M.A. 4°, paper, 333 pp., illustrated. New York: The Commonwealth Fund, 1945. $1.25.

This monograph is a report by a committee of state and local public-health administrators whose purpose was to suggest the way to cover a free society with full-time health services at the community level.

Fundamentals of Pharmacology. By Clinton H. Thienes, M.D., Ph.D., professor and head of the Department of Pharmacology, School of Medicine, University of Southern California, and attending pathologist (toxicology), Los Angeles County Hospital. *Medical Students Series.* 8°, cloth, 497 pp., with 36 illustrations and 19 tables. New York and London: Paul B. Hoeber, Incorporated, 1945. $5.75.

This new manual in the *Medical Students Series* is a practical and concise text for students and physicians. It contains the essentials of pharmacology brought up to date and correlated with modern therapeutics. Despite its conciseness, valuable clinical material has not been omitted from the text. The author makes use of a simple original classification, discussing in order drugs acting on the central and peripheral nervous systems, those acting on the muscles, diuretics, antiparasitics, hormones, iron, tissue extracts, vitamins and drugs having local action on body surfaces, including irritants, cathartics, expectorants and emetics, carminatives, emollients and demulcents, astringents and antacids. There are also short chapters on chemical diagnostic agents, drug action on cells, pharmaceutical preparations and prescription writing.

All important *U.S.P.* preparations are described, and a sufficient description of the physical and chemical properties of drugs is given to facilitate writing prescriptions. The major emphasis is laid on the dynamics of drug action, the absorption, distribution, metabolism and excretion of essential drugs and their therapeutic indications.

The text is well written and printed on good paper, with a good type, and a comprehensive, inclusive index ends the volume. The book should prove useful as a ready reference source in its field.

NOTICES

ANNOUNCEMENTS

Dr. William B. Coen announces the removal of his office to 111 Maple Street, Springfield.

Dr. Armand M. Gamboa announces his return from naval service and the opening of his office at 1075 Boylston Street, Boston.

Dr. Nelson R. Saphir announces his return from military service and will resume the practice of internal medicine at Suite 3, Hotel Canterbury, 14 Charlesgate West, Boston.

(*Notices continued on page x*)

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FACT 2 **HIGHEST IN THIAMINE CONTENT: CEREVIM**—contains 0.6 Mg. of thiamine per ounce, the highest B_1 content of the more common pre-cooked cereals.[1]

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*Based upon (1) the Report of the Council on Foods and Nutrition, J.A.M.A. 126:100, 1944, J.A.M.A. 123:902, 1943 and (2) the label statements of composition of better-known precooked cereals.

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NOTICES (*Continued from page 178*)

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, August 8

Friday, August 9

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

12:00 m.–1:00 p.m. Clinicopathological conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

Tuesday, August 13

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

Wednesday, August 14

*10:30–11:30 a.m. Medical Clinic. Isolation Building Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:30–4:00 p.m. Combined Clinic by the Medical Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

March 15–September 15. Boston University Course for Discharged Medical Officers. Page 240, issue of February 14.

September 4–7. American Congress of Physical Medicine. Page 616, issue of May 2.

September 30–October 3. Industrial Health Congress. Page 878, issue of June 27.

October 6–12. Interamerican Congress of Cardiology. Page xix, issue of June 6.

October 7–18. New York Academy of Medicine. Page 544, issue of April 18.

February 7. American Board of Obstetrics and Gynecology. Page 34, issue of July 4.

District Medical Society

PLYMOUTH

October. Jordan Hospital, Plymouth.
November. Plymouth County Hospital, South Hanson.
January. Brockton Hospital, Brockton.
February. Moore Hospital, Brockton.
March. Goddard Hospital, Brockton.
April. State Farm, Bridgewater.
May. Lakeville Sanatorium, Lakeville.

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*Literature giving confirming bibliography and physicians samples will be furnished on request.

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